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Patentanmeldung Nr. Patent application No. Demande de brevet n°

96810421.6

PRIORITY DOCUMENT

Der Präsident des Europäischen Patentamts;
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J-N. Haon
tel: (070)3403149

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Blatt 2 der Bescheinigung
Sheet 2 of the certificate
Page 2 de l'attestation

Anmeldung Nr.:
Application no.: 96810421.6
Demande n°:

Anmeldetag:
Date of filing: 24/06/96
Date de dépôt:

Anmelder:
Applicant(s):
Demandeur(s):
ROTKREUZSTIFTUNG ZENTRALLABORATORIUM BLUTSPENDEDIENST SRK
CH-3000 Bern 22
SWITZERLAND

Bezeichnung der Erfindung:
Title of the invention:
Titre de l'invention:

Polypeptides capable of forming antigen binding structures with specificity for the Rhesus D antigens, the DNA encoding them and the process for their preparation and use

In Anspruch genommene Priorität(en) / Priority(ies) claimed / Priorité(s) revendiquée(s)

Staat: State: Pays:	Tag: Date: Date.	Aktenzeichen: File no. Numéro de dépôt:

Internationale Patentklassifikation:
International Patent classification:
Classification internationale des brevets:

C12N15/13, C12N15/62, C07K16/34, A61K39/395, G01N33/80

Am Anmeldetag benannte Vertragstaaten:
Contracting states designated at date of filing: AT/BE/CH/DE/DK/ES/FI/FR/GB/GR/IE/IT/LI/LU/MC/NL/PT/SE
Etats contractants désignés lors du depôt

Bemerkungen:
Remarks:
Remarques:

Polypeptides capable of forming antigen binding structures with specificity for the Rhesus D antigens, the DNA encoding them and the process for their preparation and use

This invention relates to polypeptides forming antigen binding structures with specificity for Rhesus D antigens and especially to Fab molecules with specificity for the Rhesus D antigen. The invention also relates to their application to provide pharmacological and diagnostic compositions. The above Fab fragments when genetically engineered to be part of complete antibodies are useful for the prophylaxis of hemolytic disease of the newborn (HDN). This invention provides the novel DNA and amino acid sequences of the above polypeptides.

Thus, the antibodies can be used for the protection of Rhesus negative women before or immediately after the birth of a Rhesus positive child to prevent HDN in subsequent pregnancies.

The invention also includes the application of the said Fab molecules either alone or in combination with Fc constant regions as complete antibodies for the purposes of treating other illnesses which might benefit from anti-Rhesus D immunoglobulin e.g. treatment of idiopathic thrombocytopenic purpura (ITP).

In addition anti-Rhesus D immunoglobulin can be used after mistransfusions of Rhesus positive blood to Rhesus negative recipients in order to prevent sensitization to the Rhesus D antigen. Further the invention relates to the application of these Fab fragments and antibodies as diagnostic reagents.

HDN is the general designation for hemolytic anemia of fetuses and newborn babies caused by antibodies of the mother. These antibodies are directed against antigens on the surface of the fetal erythrocytes. These antigens can belong to the Rhesus, ABO or other blood group systems.

The Rhesus blood group system includes 5 major antigens: D, C, c, E and e (Issitt, P.D., Med. Lab. Sci. 45:395, 1988). The D antigen is the most important of these antigens as it is highly immunogenic eliciting anti-Rhesus D antibodies during Rhesus incompatible pregnancies and following transfusion of Rhesus incompatible blood. The D antigen is found in approximately 85% of Caucasians in Europe and those individuals are said to be Rhesus positive. Individuals lacking the D antigen are called Rhesus negative. The expression of the D antigen can vary due to either low antigen density, hereafter known as weak D or D^u, or due to partial antigenicity, hereafter known as partial D antigens.

The Rhesus D antigen, a membrane protein of the erythrocyte, has recently been cloned and its primary structure described (Le Van Kim, C., et al., PNAS 89:10925, 1992). Modeling studies suggest that the Rhesus D antigen has 12 transmembrane domains with only very short connecting regions extending outside the cell membrane or protruding into the cytoplasm.

The partial D phenotypes were first identified in people who carried D antigen on their red cells but who had an alloanti-D in their sera (Rose, R. R. and Sanger, R., Blood groups in man, Blackwell Scientific, Oxford, U.K. 1975; Tippett, P. et al., Vox Sanguinis. 70:123, 1996). This can be explained by regarding the D antigen as a mosaic structure with at least 9 different epitopes (epD1 to epD9). Thus in some D variant people the red cells lack part of this mosaic and antibodies are made to the missing D epitopes. Rhesus positive individuals that make antibodies against partial D antigens have been classified into six main different categories (D^{II} to D^{VII}) each having a different abnormality in the D antigen. More recently it has been shown that these D categories gave different patterns of reaction when tested against panels of human monoclonal anti-D antibodies (Tippett, P., et al., Vox Sanguinis. 70:123, 1996). The different reaction patterns identified the 9 epitopes and so define the different partial D categories. The number of epitopes present on the D antigen varies from one partial D category to another with the D^{VI} category expressing the least, epD3, 4 and 9. The D^{VI} category is clinically important as a D^{VI} woman can be immunized strongly enough to cause hemolytic disease of the newborn.

The prophylactic efficacy of anti-RhD IgG for prevention of hemolytic disease of the newborn is well established and has been in routine use for many years. As a result this severe disease has become a rarity. Nevertheless the underlying cause of the disease, i.e. RhD incompatibility between a RhD negative mother carrying a RhD positive child still remains and thus requires a continual supply of therapeutic anti-RhD IgG.

In recent years the assurance of a continual supply of anti-RhD IgG has become an increasing problem. The pool of available hyperimmune serum from alloimmunized multiparous Rhesus negative women has drastically decreased due to the success of prophylactic anti-RhD. Thus the current methods of production require repeated immunization of an increasingly reluctant pool of donors for the production of high titer antiserum (Selinger, M., Br. J. Obstet. Gynaecol. 98:509, 1991). There are also associated risk factors and technical problems such as the use of Rhesus positive red blood cells for repeated immunization carrying the risk of transmission of viral diseases like hepatitis B, AIDS and other as yet unknown viruses (Hughes-Jones, N.C., Br. J. Haematol. 70:263, 1988). Therefore an alternative method for production of anti-RhD antibodies is required.

In the past few years various alternative sources of hyperimmune serum have been tried but all are associated with disadvantages. Epstein Barr Virus (EBV) transformation of lymphocytes creating B lymphoblastoid cell lines that secrete specific antibody including against the Rhesus D antigen (Crawford et al., Lancet. 386:Feb.19th, 1983) are unstable and require extensive cloning. Also due to the low transformation efficiencies (1-3% of B cells) only a restricted range of antibody specificities can be obtained from the potential repertoire. Additionally it seems that mice do not respond to the Rhesus D antigen and thus no murine monoclonal antibodies are available which could be used for producing chimaeric or humanised antibodies. Until recently the only other alternative was production of human antibodies by the hybridoma technique which was also restricted by the lack of a suitable human myeloma cell fusion partner (Kozbor, D. and Roder, J.C., Immunol. Today. 4:72, 1983).

It is thus the object of the present invention to provide Fab fragments having a reactivity against the Rhesus D antigen as well as complete antibodies comprising the Fab fragments which are free from the above mentioned drawbacks.

In the last few years the technique of repertoire cloning and the construction of phage display libraries has opened up new possibilities to produce human antibodies of defined specificity (Williamson, R.A. et al., PNAS 90:4141, 1993). These methods were thus applied to the preparation of polypeptides capable of forming antigen binding structures with specificity for Rhesus D antigens, especially of Fab fragments having an activity against Rhesus D and partial D antigens.

The generation of human antibodies by repertoire cloning as described in recent years (Barbas III, C.F. and Lerner, R.A., Companion Methods Enzymol. 2:119, 1991) is based on isolating mRNA from peripheral B cells. This method offers the tools to isolate natural antibodies, autoantibodies or antibodies generated during the course of an immune response (Zebedee, S.L., et al., PNAS 89:3175, 1992; Vogel, M. et al., Eur.J. Immunol. 24:1200, 1994). This method relies on constructing a recombinant antibody library from a particular donor starting from the mRNA coding for immunoglobulin (Ig) molecules. As only the peripheral blood lymphocytes (PBL) can be isolated from a donor the chances of finding specific antibody producing B cells in the periphery are increased if an individual is boosted with the desired antigen shortly before harvesting the PBL (Persson, M.A.A., et al., PNAS 88:2432, 1991). The total RNA is then isolated and the mRNA of the Ig repertoire can be cloned using Ig specific primers in the polymerase chain reaction (PCR) followed by the co-expression of heavy and light chains of the Ig molecule on the surface of a filamentous phage particle thereby forming an „organism" that in analogy to a B cell can bind to an antigen. In the literature this method is also known as the combinatorial approach as it allows the independent combining of heavy and light chains to form a functional Fab antibody fragment attached to one of the tail proteins, called pIII, of a filamentous phage. Phages carrying the Fab molecules (hereafter known as Phab particles) are selected for the desired antigen specificity, by a

process known as bio-panning. The antigen can be applied to a solid support, specific Phab bind to the antigen whilst non specific Phab are washed away and finally the specific Phab are eluted from the solid support. The specific Phab are then amplified in bacteria, allowed to re-bind to the antigen on the solid support and the whole process of bio-panning is repeated.

The successive rounds of panning and amplification of selected Phab in bacteria result in an enrichment of specific Phab that can be seen from a rise in titer of colony forming units (cfu) plated out after each round of panning. Our previous experience and published data indicate that specific phage can usually be detected after 4 to 6 panning rounds (Vogel, M. et al., Eur.J. Immunol. 24:1200, 1994). In the above cited related art there is , however, no hint that the indicated steps can be used for a successful preparation of Fab fragments of anti-Rh D antibodies.

In the appended figures 1a to 17b; DNA sequences coding for variable regions (V regions) of anti Rh D Fab fragments and the corresponding polypeptide sequences are disclosed.

Fig. 18 shows the pComb3 expression system used according to the present invention.

Figs. 19 and 20 show the separate preparation of genes of the heavy and light chains of the complete antibody according to the description in example 6.

Subjects of the present invention are polypeptides capable of forming antigen binding structures with specificity for Rhesus D antigens according to the definition of claim 1. The table in claim 1 refers to the appended figures. The identification number for each sequence is given. The locations of the Rhesus D specific CDR1 (complementarity determining region 1), CDR2 and CDR3 regions are indicated in the figures and according to base pair number in the table of claim 1. Prefered polypeptides according to the invention are anti-Rhesus D antibodies which include the variable regions of the heavy and light chains according to the sequences given in

Figs. 1a -17b. The Figs. 1a, 2a, ... 17a are related to the variable regions of the heavy chain and the Figs. 1b, 2b, ... 17b are related to the variable regions of the light chain.

Further subjects of the present invention are the DNA sequences coding for antigen binding polypeptides according to the definition of claim 5. Prefered DNA sequences are those coding for variable regions of Fab fragments of anti-Rh D antibodies according to the Figs. 1a -17b. The Figs. 1a, 2a, ... 17a are related to the heavy chain and the Figs. 1b, 2b, ... 17b are related to the light chain.

A further subject of the present invention is the process for preparing recombinant Fab polypeptides according to the definition in claim 9.

Further subjects of the present invention are anti-Rh D antibodies according to the definition of claim 10, preferably anti-Rh D immunoglobulin molecules comprising the heavy and light chain variable regions according to the Figs. 1a to 17b combined with known heavy and light chain constant regions.

Further subjects of the present invention are pharmaceutical and diagnostic compositions comprising polypeptides, anti-Rh D antibodies or Fab fragments according to the invention.

The total re-amplified Phab population obtained after each panning can be tested for specificity using various methods such as ELISA and immunodot assays. It is also defined by the nature of the antigen e.g. anti-Rhesus D Phabs are detected by indirect haemagglutination using a rabbit anti-phage antibody or equivalent Coombs reagent as the cross linking antibody. Once a total Phab population has been identified as positive for the desired antigen, individual Phab clones are isolated and the DNA coding for the desired Fab molecules is sequenced. Individual Fab can then be produced by use of the pComb3 expression system which is illustrated in Fig. 18. In this system the gIII gene, coding for the tail protein pIII, is cut out from the phagemid vector pComb3. This allows production of soluble Fab in the

bacterial periplasm. Such individual Fab fragments can then be tested for antigen specificity.

The phage display approach has also been used as a means of rescuing monoclonal antibodies from unstable hybridoma cell lines. This has been reported for anti-Rhesus D antibodies (Siegel, D.L. and Silberstein, L.E., Blood. 83:2334, 1994; Dziegiel, M. et al., J. Immunol. Methods. 182:7, 1995). A phage display library constructed from non-immunized donors has also been used to select Fv fragments (i.e. variable regions of heavy and light chains, V_H and V_L) specific for human blood group antigens which included one Fv fragment reacting against the Rhesus D antigen (Marks, J.D. et al., Biotechnology. 11:1145, 1993).

Important considerations when constructing combinatorial libraries are the source of cells used for RNA extraction and the nature of the antigen used for panning. Therefore, this invention uses a hyperimmune donor who was boosted i.v. with Rhesus D^+ red blood cells (rbc). The PBL of the donor were harvested at +5 and +18 days after the i.v. boost and were used to construct 2 combinatorial libraries hereafter known as library D1 (LD1) and library D2 (LD2) respectively. Double immunofluorescence analysis of the harvested PBL, using the markers CD20 and CD38 for pan B cells and lymphoblastoid cells respectively, showed a higher than normal percentage of lymphoblastoid B cells, of plasma cell morphology. The high number of plasma cells found in the peripheral blood is most unusual as normally there are less than 1% in the periphery and probably indicates that the donor had a high percentage of circulating B cells with specificity for the Rhesus D antigen.

After construction of the library, the selection of Phabs specific for the Rhesus D antigen was achieved by bio-panning on fresh whole rbc of phenotype R1R1 (CDe/CDe) i.e. the reference cells used for Rhesus D typing. This was necessary since the Rhesus D antigen, an integral membrane protein of 417 amino acids (Le Van Kim, C. et al, PNAS 89:10925, 1992), loses its immunogenicity during purification (Paradis, G. et al, J. Immunol. 137:240, 1986) and therefore a chemically purified D antigen

cannot be bound to a solid phase for selection of immunoreactive Phabs as for other antigen specificities previously selected in this system (Vogel, M. et al., Eur.J. Immunol. 24:1200, 1994). Modelling studies have suggested that only very short connecting regions of the Rhesus D antigen extend outside the cell membrane or protrude into the cytoplasm (Chérif-Zahar, B. et al, PNAS 87:6243, 1990). Thus the parts of the RhD antigen visible to antibodies are relatively restricted and may be under conformational constraint. This aspect of the Rhesus D antigen becomes even more important when considering selection of Phabs with reactivity against the partial D phenotypes which essentially lack certain defined epitopes of the D membrane protein (Mouro, I. et al, Blood. 83:1129, 1994).

Furthermore, since whole rbc do not only express the D antigen, a series of negative absorptions had to be performed on Rhesus D negative rbc in order to absorb out those Phabs reacting with the other antigenic proteins found on the rbc.

This panning procedure performed on Phabs coming from both LD1 and LD2 librairies resulted in the isolation of 7 different Fab producing clones from library LD1 and 9 different Fab producing clones from library LD2.

The nomenclature and the figures where the sequences are listed are given in table 1.

Table 1

LIBRARY LD1 Clone No.	V_H- Sequence Figure	V_L- Sequence Figure	LIBRARY LD2 Clone No.	V_H- Sequence Figure	V_L- Sequence Figure
LD1-28	1a	1b	LD2-1	8a	8b
LD1-40	2a	2b	LD2-4	9a	9b
LD1-52	3a	3b	LD2-5	10a	10b
LD1-84	4a	4b	LD2-10	11a	11b
LD1-98	5a	5b	LD2-11	12a	12b
LD1-110	6a	6b	LD2-14	13a	13b
LD1-117	7a	7b	LD2-17	14a	14b
			LD2-18	15a	15b
			LD2-20	16a	16b

The above Fab clones show exclusive reactivity against the Rhesus D antigen, 3 of 5 D^u rbc tested and agglutinating reactivity against the Partial D phenotypes as follows: Rh33, DIII, DIVa, DIVb, DVII.

However using the above mentioned R1R1 rbc for panning of the Phabs no clones were isolated which reacted against the Partial DVI phenotype. As the serum of the original hyperimmune donor tested at the time of construction of the recombinant library, was known to react against the DVI phenotype the recombinant library should also contain the anti-DVI specificity.

In order to select for the DVI reactivity the panning conditions were changed in that different cells were used. A special donor whose rbc had been typed and were known to express the Partial DVI phenotype was used as the source of cells for re-panning the LD1 and LD2 librairies. This second series of pannings was essentially performed in the same way as the first series except for the substitution of DVI rbc for R1R1 rbc and the addition of bromelase treatment to the DVI rbc. The DVI phenotype expresses the least number of Rhesus D epitopes and it is therefore difficult to make antibodies against it. It has been reported that only 15% of unselected polyclonal anti-D and 35% of selected anti-D made by Rhesus D negative subjects reacted with DVI+ cells (Mouro, I. et al, Blood. 83:1129, 1994). Bromelase treatment which removes N- acetylneuraminic acid (sialic acid) from the rbc membrane, was performed in order to render the Rhesus DVI epitopes more accessible during the panning with the pre-absorbed Phabs.

This second series of pannings on the LD1 and LD2 librairies resulted in 1 Fab producing clone reacting with DVI+ rbc.

The nomenclature is given below:

LIBRARY LD1	V_H -Sequence figure	V_L-Sequence figure
Clone No: LD1-6-17	17a	17b

Thus a total of 17 different anti-Rhesus D Fab clones have been isolated. The DNA from these clones has been isolated and sequenced using Fluorescent Cycle Sequencing on an ABI 373A Sequencing System. The nucleotide and corresponding amino acid sequences of the said Fab clones form the basis of this invention.

The DNA sequences obtained and Fab fragments are useful for the preparation of complete antibodies having an activity against the Rhesus D antigen.

The examples which follow explain the invention in detail, without any restriction of the scope of the invention.

Example 1 describes the construction of 2 combinatorial librairies; especially the aforementioned LD1 and LD2 libraries.

Example 2 describes a series of pannings using R1R1 rbc on the said LD1 and LD2 libraries in detail.

Example 3 describes a series of pannings using bromelase treated DVI+ rbc on the said LD1 and LD2 librairies.

Example 4 describes an indirect haemagglutination assay using a rabbit anti-phage antibody, as an equivalent Coombs reagent, to monitor the enrichment and specificity of Rhesus D specific Phabs after panning.

Example 5 describes the preparation and purification of Fab antibody fragments for application as diagnostic reagents.

Example 6 describes the preparation of complete anti-Rhesus D immunoglobulins using the sequences of the present invention.

Example 1

Construction of the recombinant LD1 and LD2 librairies

a) Source of the lymphocytes

A male adult who was a member of the volunteer pool of hyperimmune Rhesus D donors was given an i.v. boost of 2 ml of packed rbc from a known male donor of blood group O RhD$^+$. The PBL were harvested at +5 and +18 days after the boost and the mononuclear cells (MNC) isolated by Ficoll gradient centrifugation (Lymphoprep, Pharmacia, Milwaukee, WI). The +5 day MNC were used directly for RNA preparation using a phenol-chloroform guanidinium isothiocyanate procedure (Chomczynski, P. and Sacchi, N., Anal. Biochem. 162:156, 1987). The +18 day MNC were first cultured for 3 days in RPMI-1640 medium (Seromed, Basel) containing 10^3 U/ml of IL-2 (Sandoz Research Center, Vienna, Austria) and 10 µg/ml of pokeweed mitogen (PWM; Sigma L9379, Buchs, Switzerland) before extracting RNA.

Immunofluorescence analysis of donor lymphocytes +5 days after rbc i.v. boost

Cell Surface Antigen	% Positive cells	Cell Surface Antigen	% Positive cells
CD20	15	CD8	12
CD38	20	CD25	7.6
CD20/38	15	CD57	12.5
CD3	47	CD14	6
CD4	34	HLA-DR	18

b) Construction of Library

Two separate libraries were constructed called LD1 and LD2 (as detailed above) corresponding to the cells harvested at +5 days and +18 days (finally +21 days including the +3 days PWM stimulation) after the i.v. boost

respectively. Total RNA was then prepared from these cells using a phenol-chloroform guanidinium isothiocyanate method. From this RNA, 10 μg were used to make cDNA using an oligo(dT) primer (400 ng) and reverse transcribed with M-MuLV reverse transcriptase according to the conditions specified by the supplier (Boehringer Mannheim Germany). PCR amplification was performed as described in Vogel, M. et al., E.J. of Immunol. 24:1200, 1994. Briefly, 100 μl PCR reaction contained Perkin-Elmer buffer with 10 mM $MgCl_2$, 5 μl cDNA, 150 ng of each appropriate 5′ and 3′ primer, all four dNTP at 200 μM each and 2 U/ml Taq Polymerase (Perkin Elmer, NJ). The PCR amplification of the heavy and light chains of the Fab molecule was performed separately with a set of primers from Stratacyte (details given below). For the heavy chain six upstream primers were used that hybridize to each of the six families of the V_H genes whereas one kappa and one lambda chain primer were used for the light chain. The downstream primers were designed to match the hinge region of the constant domains γ1 and γ3 for the heavy chain. For the light chain the downstream primers were matched to the 3′ end of kappa and lambda constant domains. The heavy and light chain PCR products were pooled separately, gel purified and cut with Xho1/Spe1 and Sac1/ Xba1 restriction enzymes (Boehringer Mannheim), respectively. After digestion the PCR products were extracted once with phenol : chloroform : isoamylalcohol and purified by gel excision. The insertion of the Xho1/Spe1 digested Fd fragment and subsequent ligation of the Sac1/Xba1 digested light chain into the pComb3 vector, the transformation into XL1-Blue cells, and the production of phages were performed as described by (Barbas III, C.F. and Lerner, R.A., Companion Methods Enzymol. 2:119, 1991).

After transformation of the XL1-Blue E.coli cells samples were withdrawn and titrated on plates to determine the library size. These results indicated expression libraries of 7.5×10^6 and 7.7×10^6 cfu (colony forming units) for LD1 and LD2 respectively.

c) PCR Primers

VHI 5'-CAC TCC CAG GTG CAG CTG CTC GAG TCT GG-3'

VHII 5'-GTG CTG TCC CAG GTC AAC TTA CTC GAG TCT GG-3'

VHIII 5'-GTC CAG GTG GAG GTG CAG CTG CTC GAG TCT GG-3'
VHIV 5'-GTC CTG TCC CAG GTG CAG CTG CTC GAG TCG GG-3'
VHV 5'-GTC TGT GCC GAG GTG CAG CTG CTC GAG TCT GG-3'
VHVI 5'-GTC CTG TCA CAG GTA CAG CTG CTC GAG TCA GG-3'
CHI(gI) 5'-AGC ATC ACT AGT ACA AGA TTT GGG CTC-3'
VL(k) 5'-GT GCG AGA TGT GAG CTC GTG ATG ACC CAG TCT CCA-3'
CL(k) 5'-T CCT TCT AGA TTA CTA ACA CTC TCC CCT GTT GAA GCT CTT TGT GAC GGG CGA ACT C-3'
VL(l) 5'C TGC ACA GGG TCC TGG GCC GAG CTC GTG GTG ACT CA-3'
CL(l) 5'G CAT TCT AGA CTA TTA TGA ACA TTC TGT AGG GGC-3'

d) Vectors and bacterial strains

The pComb3 vector used for cloning of the Fd and the light chain was obtained from the Scripps Research Institute La Jolla, CA; (Barbas III, C.F. and Lerner, R.A., Companion Methods Enzymol. 2:119, 1991). The *Escherichia coli* strain XL1-Blue used for transformation of the pComb3 vector and the VCSM13 helper phage were purchased from Stratacyte (La Jolla, CA).

Example 2

Selection of Rhesus D Phabs from LD1 and LD2 librairies on R1R1 rbc

a) Absorption and Bio-Panning

A series of three negative absorptions on rbc group O Rh negative were performed for each panning round before positive selection on rbc group O Rh positive (R1R1). Fresh rbc were collected in ACD (acid citrate dextrose) anticoagulant and washed 3 times in 0.9% NaCl. The rbc were counted in Hayems solution and adjusted to $40x10^6$/ml. Absorption : 1 ml of phage preparation in PBS/3%BSA was added to rbc group O Rh negative pellet ($16x10^6$ rbc) in 12 ml tubes (Greiner 187261, Reinach, Switzerland) and incubated at RT for 30 min. with careful shaking. All tubes were pre-blocked in PBS/3% BSA for a minimum of 1hr at RT. The rbc were pelleted by centrifuging for 5 min. 300 x g at 4°C. The resulting phage supernatant was

carefully harvested and the process repeated twice more. After the final absorption the phage supernatant was added to the rbc group O Rh positive pellet ($16x10^6$ rbc) and again incubated at RT for 30 min. with gentle shaking. Then the rbc were washed at least 5 times in 10 ml ice cold PBS, centrifuged 5 min. 300 x g at 4°C, followed by elution with 200 µl of 76 mM citric acid pH 2.8 for 6 min. at R.T. and neutralisation with 200 µl 1M Tris. The rbc were centrifuged 300 x g, 5 min. at 4°C and the resulting supernatant containing the eluted phages was carefully removed and stored with carrier protein (0.3% BSA) at 4°C ready for re-amplification.

Selection of Rhesus D+ Phabs from the LD1 and LD2 librairies on R1R1 rbc

Panning Round No.[a)]	No. of eluted Rhesus D specific phages Library D1 cfu	Library D2 cfu
1	$8x10^6$	$4.6x10^7$
2	$6x10^7$	$1.4x10^7$
3	$1x10^8$	$7.9x10^7$
4	$3x10^8$	$1.3x10^8$
5	$3x10^8$	$1x10^8$
6	nd	$2.8x10^8$

a) For each round 10^{12} Phabs were incubated in tubes with rbc Group O Rhesus negative (absorption phase) followed by elution from rbc Group O Rhesus positive (R1R1)

nd = not done
cfu = colony forming units

Example 3

Selection of Rhesus D Phabs from LD1 and LD2 librairies on DVI+ rbc

a) Absorption on rbc group O Rh negative

A series of three negative absorptions on rbc group O Rh negative were performed for each panning round before positive selection on rbc group O Rh DVI positive. Fresh rbc were collected in ACD anticoagulant and washed 3 times in 0.9% NaCl. The rbc were counted in Hayems solution and adjusted to $40x10^6$/ml. Absorption : 1 ml of phage preparation in PBS/3%BSA was added to rbc group O Rh negative pellet ($16x10^6$) in 12 ml tubes (Greiner 187261, Reinach, Switzerland) and incubated at RT for 30 min. with careful shaking. All tubes were pre-blocked in PBS/3% BSA for a minimum of 1hr at RT. The rbc were pelleted by centrifuging for 5 min. 300 x g at 4°C. The resulting phage supernatant was carefully harvested and the process repeated twice more. Treatment of the rbc group O Rhesus DVI+ with the enzyme bromelase was performed at this stage in order to enhance accessibility of the antigens.

b) Treatment of rbc Rhesus DVI+ with bromelase

Bromelase 30 (Baxter, Düdingen, Switzerland) was used to treat rbc Rhesus DVI+ in the same proportions as used in a routine haemagglutination assay, i.e. 10 µl bromelase per $2x10^6$ rbc. Thus 80 µl of bromelase was added to $16x10^6$ DVI+ rbc and incubated at 37°C for 30 min. followed by washing 3 times in 0.9% NaCl, re-counting in Hayems solution and adjusting to $40x10^6$/ml in PBS/3% BSA ready for Phab panning.

c) Bio-Panning on bromelase treated Rhesus DVI+ rbc

After the final absorption the phage supernatant was added to the enzyme treated rbc group O Rh DVI+ pellet ($16x10^6$) and again incubated at RT for 30 min. with gentle shaking. Then the rbc were washed at least 5 times in 10 ml ice cold PBS, centrifuged 5 min. 300 x g at 4°C, followed by elution with 200 µl of 76 mM citric acid pH 2.8 for 6 min. at R.T. and neutralisation with 200 µl 1M Tris. The rbc were centrifuged 300 x g, 5 min. at 4°C and the

resulting supernatant containing the eluted phages was carefully removed and stored with carrier protein (0.3% BSA) at 4°C ready for re-amplification.

Selection of Rhesus D Phabs from LD1 and LD2 librairies on Rhesus DVI+ red blood cells

Panning Round No.[a)]	No. of eluted Rhesus D specific phages Library LD1 cfu	Library LD2 cfu
1	$5x10^7$	$4.6x10^7$
2	$1.8x10^7$	$1.4x10^7$
3	$4x10^8$	$7.9x10^7$
4	$6.8x10^8$	$1.3x10^8$
5	$5.8x10^8$	$1x10^8$

a) For each round 10^{12} Phabs were incubated in tubes with rbc Group O Rhesus negative (absorption phase) followed by elution from rbc Group O Rhesus DVI+

Example 4

Monitoring of the panning rounds and determination of the specificity of the enriched Phabs using a rabbit anti-phage antibody

Indirect haemagglutination assay

Freshly collected rbc of different ABO and Rhesus blood groups were washed 3 times in 0.9% NaCl and adjusted to a 3-5% solution (45-$50x10^7$/ml) in either 0.9% NaCl or PBS/3% BSA. For each test condition 50 µl rbc and 100 µl test (precipitated and amplified phage or control antibodies) were incubated together in glass blood grouping tubes (Baxter, Düdingen, Switzerland) for 30 min. at 37°C. The rbc were washed 3 times in 0.9% NaCl and then incubated with 2 drops of Coombs reagent (Baxter, Düdingen, Switzerland) for positive controls or with 100 µl of 1/1000 diluted rabbit anti-phage antibodies (made by immunising rabbits with phage VCSM13

preparation, followed by purification on an Affi-Gel Blue column and absorption on E. coli to remove E. coli-specific antibodies). The tubes were incubated for 20 min at 37°C, centrifuged 1min at 125xg and rbc examined for agglutination by careful shaking and using a magnifier viewer.

When purified Fab were tested for agglutination an affinity purified anti-Fab antibody (The Binding Site, Birmingham, U.K.) was used instead of the rabbit anti-phage antibody.

Monitoring of Phabs from LD1 and LD2 librairies by indirect haemagglutination after Panning on R1R1 rbc

Phab sample Panning Round	Library LD1 tested on rbc O Rh D+ (a)	Library LD2
No. 4		
undiluted	+	+
1/4	+	+/-
1/20	-	-
No.5		
undiluted	++	+
1/4	++	+
1/20	-	-
No. 6		
undiluted	nd	+++
1/4	nd	++
1/20	nd	nd
Helper phage (b)		
undiluted, 1/4, 1/20	-	-

a) Indirect haemagglutination was performed in glass tubes using 50 µl rbc ($40x10^7$/ml) and 100 µl Phabs starting at $4x10^{11}$/ml. After 30 min. at 37°C the rbc were washed 3 times and further incubated for 20 min. at 37°C with a 1/1000 dilution of rabbit anti-phage antibody.

b) The M13 helper phage was used as a negative control and showed no non-specific agglutination due to the phage particle alone.

Agglutination was scored by visual assessment from +++ (strong agglutination) descending to - (no agglutination). nd = not done

Reaction Pattern of Fab Rhesus D Clones, resulting from R1R1 rbc panning, against Partial D Variants

	Partial D Variants					
(a) Reaction Pattern of Clones from Library LD2	Rh33	DIII	DIVa	DIVb	DVI	DVII
Pattern 1 n=2 (b)	+++	nd	+++	+++	-	+++
Pattern 2 n=1	-	+++	-	+	-	+++
Pattern 3 n=1	-	+++	+++	+	-	+++
Pattern 4 n=2	-	nd	+++	+++	-	+++
Pattern 5 n=1	+++	+++	+++	+++	-	+++
Pattern 6 n=1	-	+++	-	-	-	+++
Pattern 7 n=1	-	+++	+++	-	-	+++

a) soluble Fab preparations were made of each clone (as detailed in example 5) followed by indirect haemagglutination on the above panel of D variants
b) n represents number of clones in each reaction pattern
Pattern 1: clones: LD2-1,14
Pattern 2: clone: LD2-4
Pattern 3: clone : LD2-17
Pattern 4: clones: LD2-5,10
Pattern 5: clone: LD2-18
Pattern 6: clone: LD2-11
Pattern 7: clone: LD2-20
nd = not done

Reaction Pattern of Rhesus D Clones against Partial DVI Variant

Only the LD1-6-17 clone resulting from panning against DVI+rbc reacted with DVI+ and R1R1 rbc in the indirect haemagglutination assay using rabbit anti phage antibody as the Coombs equivalent reagent and in the presence of Enlisst (Baxter).

Example 5

Preparation and purification of Fab antibody fragments for application as diagnostic reagents

After the bio-panning procedures detailed in Examples 2 and 3 a phage population which showed specific agglutination on Rhesus D+ rbc was selected and used to prepare phagemid DNA. More precisely the Phabs selected on R1R1 rbc were used after the 5th and 6th rounds of bio-panning for LD1 and LD2 libraries respectively and after the 5th bio-panning on DVI+ rbc for isolation of the LD1-6-17 clone. In order to produce soluble Fab, the sequence gIII coding for the pIII tail protein of the phage particle must be deleted.

Phagemid DNA was prepared using a Nucleotrap kit (Machery-Nagel) and the gIII sequence was removed by digesting the so isolated phagemid DNA with Nhe1/Spe1 as described (Burton, D.R., et al.,PNAS, 1989). After transformation into XL1-Blue individual clones were selected (nomenclature given in table 1) and grown in LB (Luria Broth) containing 50 µg/ml carbenicillin at 37°C to an OD of 0.6 at 600 nm. Cultures were induced with 2 mM isopropyl β-D-thiogalactopyranoside (IPTG) (Biofinex, Praroman, Switzerland) and grown overnight at 37°C. The whole culture was spun at 10,000xg for 30 min. at 4°C to pellet the bacteria. The bacterial pellet was treated with a lysozyme/DNase solution to liberate the Fab fragments inside the cells. As some Fab were released into the culture supernatant this was also harvested separately. These Fab preparations were then pooled and precipitated with 60% ammonium sulphate (Merck, Darmstadt, Germany) to concentrate the Fab followed by extensive dialysis in phosphate buffered saline (PBS) and ultracentrifugation at 200,000xg to pellet any insoluble complexes. The Fab preparations were then purified on a ceramic hydroxyapatite column (HTP Econo cartridge, BioRad, Glattbrugg, Switzerland) using a gradient elution of PBS (Buffer A) and PBS + 0.5M NaCl (Buffer B). The linear gradient was programmed to increase from 0-100% Buffer B in 40 min. The Fab was eluted as a single peak between 40-60% Buffer B. The positive fractions as identified by immunodot assay using an

anti-Fab peroxidase conjugate (The Binding Site, Birmingham, U.K.) were pooled, concentrated using polyethylene glycol and extensively dialysed against PBS. The positive fractions from the hydroxyapatite column for each clone were used in a classical indirect haemagglutination assay in glass tubes using either the standard Coombs reagent (Baxter Diagnostics AG Dade, anti-human serum) or an anti-Fab (The Binding Site, Birmingham, U.K.) as the cross linking reagent. These Fab of defined specificity on the Partial D variants as shown on page 18 can be used to type rbc of unknown Partial D phenotype.

Example 6

Construction of complete immunoglobulin genes

The LD2-14 heavy chain V gene (V_H gene) was amplified from the anti-Rhesus D-Fab-encoding plasmid LD2-14 with the polymerase chain reaction (PCR) using gene-specific primers. The 5'-primer had the sequence 5'-AGGTGTCGACGCACAGGTGAAACTGCTCGAG-3' whereas the 3'-primer was of the sequence: 5'-GAGGAGACGGTGACCGTGGT-3'. The PCR reaction was performed with Taq DNA Polymerase and the buffer solution from Boehringer Mannheim (Mannheim, Germany) at the conditions recommended by the manufacturer including 60 pmol of each primer and the four deoxynucleotides at a concentration of 0.25 μM each. The reaction was run for 35 cycles with the following temperature steps: 60 s at 94°C (extended by 5 min. during the first cycle), 75 s at 55°C and 90 s at 72°C (extended by 5 min. during the last cycle). The PCR product was purified with the QIAquick kit from Qiagen, Basel, Switzerland, digested with the restriction enzymes *Sal* I and *Bst*E II, extracted with phenol, purified by preparative agarose gel electrophoresis, concentrated by precipitation with ethanol and solubilized in a minimal volume of LTE buffer (10 mM Tris-HCl pH 8.0, 0.1 mM EDTA).

Vector # 150 (Sandoz Pharma, Basel) which contained an irrelevant intact human genomic immunoglobulin V_H gene was cut with *Sal* I and *Bst*E II, treated with calf intestinal phosphatase, extracted twice with

phenol, once with chloroform/isoamylalcohol (24:1), concentrated by precipitation with ethanol and solubilized in a minimal volume of LTE. 100 ng of this vector and 15 ng of the digested and purified PCR product were ligated according to the recommendations of the manufacturer in a total volume of 20 µl (Ligase and buffer concentrate from Boehringer Mannheim (Mannheim)). The ligase was inactivated for 10 min. at 65°C, the reaction mix diluted to 100 µl with H_20 and 3 µl of the diluted solution were electroporated with a GenePulser (BioRad, Gaithersburg) into 40 µl of competent E. coli JA221 according to the recommendations of the manufacturer (0.1 cm cuvettes, 1.8 kV, 200 Ω, 25 µFD), diluted with SOC medium, incubated at 37°C without shaking for 1 h and plated on LB plates containing ampicillin (50 µg/ml). Plasmid-minipreps of the resulting colonies were checked with restriction digests for the presence of the appropriate insert.

With this procedure, the irrelevant resident V_H gene in vector # 150 was replaced by the amplified anti-Rhesus D V_H sequence and yielded plasmid # 150-LD2-14. The structure of the resulting genomic immunoglobulin V_H gene construct was confirmed by sequencing, cut out by digestion with *Eco*R I and *Bam*H I and gel purified as described above for the PCR product. Expression vector # 10 (Sandoz Pharma, Basel) containing the human genomic immunoglobulin Cγ1 gene segment was also digested with *Eco*R I and *Bam*H I, treated with calf intestinal phosphatase, extracted with phenol, concentrated by precipitation with ethanol as described above, ligated with the *Eco*R I/*Bam*H I-V_H gene segments previously obtained from plasmids # 150-LD2-14 and transfected into E. coli JA221 as described above. This second cloning step yielded a complete anti-Rhesus D heavy chain immunoglobulin gene in plasmid # 10-LD2-14 (Figures 19 and 20).

The LD2-14 light chain V gene (V_L gene) was amplified from the same anti-Rhesus D-Fab plasmid LD2-14 by PCR using gene-specific primers. The 5'-primer had the sequence:
5'-GGTACGCGTTGTGAGCTCGTGATGACCCAG-3'
whereas the 3'-primer was of the sequence
5'-TTTGATCTCAAGCTTGGTCCCAGGGCC-3'.

PCR reaction, product purification and subsequent cloning steps were performed as described for the V_H gene, except that the appropriate light chain vectors were used. Briefly, the V_L PCR product was digested with the restriction enzymes *Mlu*I and *Hin*d III, extracted with phenol, purified from an agarose gel, ligated into vector # 151 (Sandoz Pharma, Basel) and propagated in E. coli JA221. This vector had been cut with *Mlu*I and *Hin*d III, treated with calf intestinal phosphatase, extracted with phenol and concentrated by precipitation with ethanol. Plasmid # 151 contained an irrelevant intact human genomic immunoglobulin V_L gene. With this procedure, the irrelevant resident V_L gene was replaced by the amplified anti-Rhesus D sequence and yielded plasmids # 151-LD2-14. The structure of the resulting genomic construct was confirmed by sequencing, cut out by digestion with *Eco*R I and *Xba* I and gel purified as described above. Subsequently, expression vector # 98 (Sandoz Pharma, Basel, Switzerland) containing the human genomic immunoglobulin Cκ gene segment was digested with *Eco*R I and *Xba* I, treated with calf intestinal phosphatase, extracted with phenol, concentrated by precipitation with ethanol, ligated with the *Eco*R I/*Xba* I-V_L gene segment obtained from plasmid # 151-LD2-14 and transfected into E. coli JA221. This procedure yielded a complete anti-Rhesus D light chain immunoglobulin gene in plasmid # 98-LD2-14.

Restriction digests confirmed the structure of the expression constructs for LD2-14 heavy and light chain. The mouse myeloma cell line SP2/0-Ag 14 (ATCC CRL 1581) was cotransfected by electroporation with the plasmids # 10-LD2-14 and # 98-LD2-14. The electroporation was performed as follows: Exponentially growing cells were washed twice and suspended in phosphate buffered sucrose (272 mM sucrose, 1 mM $MgCl_2$, 7 mM NaH_2PO_4, pH 7.4) at a density of 2×10^7 cells/ml. 0.8 ml of cells were added to a 0.4 cm cuvette, mixed with 15 µg of linearized plasmids # 10-LD2-14 and # 98-LD2-14, held on ice for 15 min., electroporated with 290 Volts, 200 Ω, 25 µFD, put back on ice for 15 min., transferred to a T75 cell culture flask with 20 ml of cold RPMI 1640 medium (10% heat inactivated fetal bovine serum, 50 µM beta-mercaptoethanol), left for 2 h at room temperature and then incubated for 60 h at 37°C. After this period, the cells were transferred to 50 ml of medium containing 1 mg/ml G418 for selection. Two weeks later, all non-

transformed cells had died and the supernatants tested positive for the presence of human IgG/κ by an enzyme linked immuno-sorbent assay (ELISA). The cultures were cloned by limiting dilution in microtiter plates and the supernatants quantitated by ELISA. The best producer clone was used for production cultures. From 2 - 3 liters of culture supernatant the antibodies were purified by affinity chromatography on a Protein G Sepharose (Pharmacia, Uppsala) according to the recommendations of the manufacturer. Briefly, the supernatant was diluted with 1 volume of 10 mM phosphate buffer pH 7.0, 0.02% NaN_3 and pumped over a column with 2 ml of Protein G Sepharose. The column was washed with 30 ml of 10 mM phosphate buffer pH 7.0, 0.02% NaN_3 and the bound antibodies were eluted with 0.1 M Glycine-HCl pH 2.0, 0.02% NaN_3 and immediately neutralised with solid $NaHCO_3$. These antibodies (rD2-14) were positive for agglutination of Rhesus D positive and negative for Rhesus D negative red blood cells.

The same procedure was used to produce complete recombinant antibodies from the other clones from LD1 and LD2. Because of sequence diversity, for some clones different PCR primers were synthesized. For the heavy chain this was LD1-84, where the sequence of the 5'-primer was 5'-AGGTGTCGACGCACAGGTAAACTGCTCGAG-3'.) For the light chain the 5'-primer was the same as for LD2-14 noted above (except for LD2-1, -10, where the sequence was 5'-GGTACGCGTTGTGA-GCTCGTGGTGACTCAG-3') whereas the 3'-primer was of the sequence 5'-TTTGATTTCAAGC-TTGGTCCCTTGGCC-3', except for some clones where the following 3'-primers were used:

LD1-52, -98: 5'-TTTGATCTCAAGCTTGGTCCCAGGGCC-3',

LD1-40: 5'-TTTGATCTCAAGCTTTGTCCCTTGGCC-3',

LD1-84: 5'-TTTGATGTCAAGCTTGGTCCCCCGGCC-3',

LD2-11: 5'-TTTGATCTGAAGCTTGGTCCCCTGCCC-3'.

LD2-1, -10: 5'-TAGGACGGTAAGCTTGGTCCCTCCGCC-3').

The cloning steps for the production of complete antibody heavy and light chain genes were the same as those described above for LD2-14. Expression in SP2/0-Ag14 cells yielded antibodies with the same anti-Rhesus D specificities as the Fab expressed in E. coli.

Claims

1. Polypeptides capable of forming antigen binding structures with specificity for Rhesus D antigens which include Rhesus D-specific CDR 1, CDR 2 and CDR 3 regions of the amino acid sequences V_H and V_L with the identification numbers according to the figures given in the table below:

	V_H				V_L			
Identification No.	Figure	CDR 1 base pair No.	CDR 2 base pair No.	CDR 3 base pair No.	Figure	CDR 1 base pair No.	CDR 2 base pair No.	CDR 3 base pair No.
LD1-28	Fig. 1a	91-104	148-198	295-342	Fig. 1b	64-96	142-162	259-288
LD1-40	Fig. 2a	91-105	148-198	295-342	Fig. 2b	64-96	142-162	259-288
LD1-52	Fig. 3a	91-105	148-198	295-342	Fig. 3b	64-96	142-162	259-288
LD1-84	Fig. 4a	91-105	148-198	295-342	Fig. 4b	64-96	142-162	259-285
LD1-98	Fig. 5a	91-105	148-198	295-342	Fig. 5b	64-96	142-162	259-288
LD1-110	Fig. 6a	91-105	148-198	295-342	Fig. 6b	64-96	142-162	259-285
LD1-117	Fig. 7a	91-105	148-198	295-345	Fig. 7b	64-96	142-162	259-288
LD2-1	Fig. 8a	91-105	148-198	295-342	Fig. 8b	61-99	145-165	262-294
LD2-4	Fig. 9a	91-105	148-198	295-342	Fig. 9b	64-96	142-162	259-282
LD2-5	Fig.10a	91-105	148-198	295-342	Fig. 10b	64-96	142-162	259-288
LD2-10	Fig. 11a	91-105	148-198	298-345	Fig. 11b	61-102	148-168	265-294
LD2-11	Fig. 12a	91-105	148-198	295-342	Fig. 12b	64-96	142-162	259-285
LD2-14	Fig. 13a	91-105	148-198	295-342	Fig. 13b	64-96	142-162	259-285
LD2-17	Fig. 14a	91-105	148-198	295-342	Fig. 14b	64-96	142-162	259-285
LD2-18	Fig. 15a	91-105	148-198	295-342	Fig. 15b	64-96	142-162	259-288
LD2-20	Fig. 16a	91-105	148-198	295-342	Fig. 16b	64-96	142-162	259-285
LD1-6-17	Fig. 17a	91-105	148-198	295-351	Fig. 17b	64-96	142-162	259-285

2. Polypeptides according to claim 1 which include regions with the amino acid sequences V_H and V_L and have identification numbers according to the figures given in the table of claim 1.

3. Polypeptides according to claim 1 or 2 characterised as antigen binding Fab fragments.

4. Polypeptides according to claim 1 or 2 comprising immunoglobulin heavy and light chains capable of forming complete anti-Rhesus D antibodies.

5. DNA sequences coding for polypeptides capable of forming antigen binding structures with specificity for Rhesus D antigens which include regions with the Rhesus D-specific CDR 1, CDR 2 and CDR 3 segments of the DNA sequences V_H and V_L with the identification numbers according to the figures given in the table below, and functional equivalents thereof:

	V_H				V_L			
Identification No.	Figure	CDR 1 base pair No.	CDR 2 base pair No.	CDR 3 base pair No.	Figure	CDR 1 base pair No.	CDR 2 base pair No.	CDR 3 base pair No.
LD1-28	Fig. 1a	91-104	148-198	295-342	Fig. 1b	64-96	142-162	259-288
LD1-40	Fig. 2a	91-105	148-198	295-342	Fig. 2b	64-96	142-162	259-288
LD1-52	Fig. 3a	91-105	148-198	295-342	Fig. 3b	64-96	142-162	259-288
LD1-84	Fig. 4a	91-105	148-198	295-342	Fig. 4b	64-96	142-162	259-285
LD1-98	Fig. 5a	91-105	148-198	295-342	Fig. 5b	64-96	142-162	259-288
LD1-110	Fig. 6a	91-105	148-198	295-342	Fig. 6b	64-96	142-162	259-285
LD1-117	Fig. 7a	91-105	148-198	295-345	Fig. 7b	64-96	142-162	259-288
LD2-1	Fig. 8a	91-105	148-198	295-342	Fig. 8b	61-99	145-165	262-294
LD2-4	Fig. 9a	91-105	148-198	295-342	Fig. 9b	64-96	142-162	259-282
LD2-5	Fig.10a	91-105	148-198	295-342	Fig. 10b	64-96	142-162	259-288
LD2-10	Fig. 11a	91-105	148-198	298-345	Fig. 11b	61-102	148-168	265-294
LD2-11	Fig. 12a	91-105	148-198	295-342	Fig. 12b	64-96	142-162	259-285
LD2-14	Fig. 13a	91-105	148-198	295-342	Fig. 13b	64-96	142-162	259-285
LD2-17	Fig. 14a	91-105	148-198	295-342	Fig. 14b	64-96	142-162	259-285
LD2-18	Fig. 15a	91-105	148-198	295-342	Fig. 15b	64-96	142-162	259-288
LD2-20	Fig. 16a	91-105	148-198	295-342	Fig. 16b	64-96	142-162	259-285
LD1-6-17	Fig. 17a	91-105	148-198	295-351	Fig. 17b	64-96	142-162	259-285

6. DNA sequences according to claim 5 which include regions with the DNA sequences V_H and V_L with the identification numbers according to the figures given in claim 5.

7. DNA sequences according to claim 5 or 6 coding for polypeptides capable of forming antigen binding Fab fragments.

8. DNA sequences according to claim 5 or 6 coding for polypeptides capable of forming complete anti-Rhesus D antibodies.

9. A process for preparing recombinant polypeptides capable of forming antigen binding structures, e.g. Fab fragments, with specificity for Rhesus D antigens which process comprises the following steps in sequential order:

a) boosting of an individual capable of forming anti-Rhesus D antibodies with Rhesus D positive red blood cells,

b) isolating mononuclear cells from the individual,

c) isolating total RNA from the mononuclear cells,

d) preparing a cDNA by using an oligo(dT)primer and reverse transcribing of the mRNA with M-MuLV reverse transcriptase and amplifying the cDNA repertoire by a polymerase chain reaction using immunoglobulin gene family specific primers,

e) creating a phage display library by inserting the DNA coding for the heavy and light chain of the Fab polypeptide into a phagemid vector; the DNA for the heavy chain is inserted in frame to the gene coding for the phage protein pIII which allows the expression of a Fab pIII fusion protein on the surface of the phage,

f) transforming bacterial cells with the obtained recombinant plasmids, cultivating of the transformed bacterial cells and co-expression of the heavy and the light chain of a Fab on filamentous phage particles,

g) amplifying the Fab-carrying phage in bacteria,

h) selecting individual phage clones by several rounds of panning on Rhesus positive red blood cells.

i) isolating the plasmid DNA from the selected clones and cutting out the gIII gene,

j) transforming bacterial cells with the obtained plasmid, cultivating of the transformed bacterial cells expressing the Fab, and isolating the Fab fragments.

10. Anti-Rhesus D antibodies having heavy and light chain variable regions comprising the Rhesus D-specific CDR 1, CDR 2 and CDR 3 sequences of the amino acid sequences V_H and V_L given the identification numbers as indicated in the table below:

	V_H				V_L			
Identification No.	**Figure**	**CDR 1 base pair No.**	**CDR 2 base pair No.**	**CDR 3 base pair No.**	**Figure**	**CDR 1 base pair No.**	**CDR 2 base pair No.**	**CDR 3 base pair No.**
LD1-28	Fig. 1a	91-104	148-198	295-342	Fig. 1b	64-96	142-162	259-288
LD1-40	Fig. 2a	91-105	148-198	295-342	Fig. 2b	64-96	142-162	259-288
LD1-52	Fig. 3a	91-105	148-198	295-342	Fig. 3b	64-96	142-162	259-288
LD1-84	Fig. 4a	91-105	148-198	295-342	Fig. 4b	64-96	142-162	259-285
LD1-98	Fig. 5a	91-105	148-198	295-342	Fig. 5b	64-96	142-162	259-288
LD1-110	Fig. 6a	91-105	148-198	295-342	Fig. 6b	64-96	142-162	259-285
LD1-117	Fig. 7a	91-105	148-198	295-345	Fig. 7b	64-96	142-162	259-288
LD2-1	Fig. 8a	91-105	148-198	295-342	Fig. 8b	61-99	145-165	262-294
LD2-4	Fig. 9a	91-105	148-198	295-342	Fig. 9b	64-96	142-162	259-282
LD2-5	Fig.10a	91-105	148-198	295-342	Fig. 10b	64-96	142-162	259-288
LD2-10	Fig. 11a	91-105	148-198	298-345	Fig. 11b	61-102	148-168	265-294
LD2-11	Fig. 12a	91-105	148-198	295-342	Fig. 12b	64-96	142-162	259-285
LD2-14	Fig. 13a	91-105	148-198	295-342	Fig. 13b	64-96	142-162	259-285
LD2-17	Fig. 14a	91-105	148-198	295-342	Fig. 14b	64-96	142-162	259-285
LD2-18	Fig. 15a	91-105	148-198	295-342	Fig. 15b	64-96	142-162	259-288
LD2-20	Fig. 16a	91-105	148-198	295-342	Fig. 16b	64-96	142-162	259-285
LD1-6-17	Fig. 17a	91-105	148-198	295-351	Fig. 17b	64-96	142-162	259-285

11. Anti-Rhesus D antibodies according to claim 10 with the amino acid sequences V_H and V_L and the identification numbers according to the figures, as indicated in the table of claim 10.

12. Anti-Rhesus D antibodies according to claim 10 or 11 wherein the immunoglobulin constant regions are of at least one of the defined isotypes IgG1, IgG2, IgG3 or IgG4.

13. A process for preparing complete anti-Rhesus D antibodies according to one of the claims 10 to 12, comprising in sequential order the steps of

a) amplifying separately the members of a pair of a heavy chain V gene segment and a light chain V gene segment containing Rhesus D-specific CDR 1, CDR 2 and CDR 3 regions as depicted in Figs. 1a - 17a and 1b - 17b, respectively, from an anti-Rhesus D-Fab-encoding plasmid by carrying out a polymerase chain reaction with specific primers,

b) preparing separately the genes of a complete anti-Rhesus D immunoglobulin heavy chain and a complete anti-Rhesus D immunoglobulin light chain in suitable plasmids containing the immunoglobulin constant region gene segments coding for either one of the human γ1, γ2, γ3 and γ4 heavy chains and for the human κ or λ light chain and transforming the obtained plasmids separately in suitable E. coli bacteria, and

c) cotransfecting the obtained plasmids into a suitable mouse myeloma cell line, cultivating of the cells, separating the non-transformed cells, cloning of the cultures, selecting the best producing clone, using it as a production culture and isolating the complete antibodies from the supernatant of the cell culture.

14. A pharmaceutical composition comprising at least one polypeptide according to the definition of claim 1 or 2 or at least one anti-Rhesus D antibody according to one of the claims 10 to 12 for the prophylaxis

of haemolytic disease of the newborn, for the treatment of idiopathic thrombocytopenic purpura and mistransfusions of Rhesus incompatible blood.

15. A diagnostic composition for Rhesus D typing comprising Fab fragments according to claim 3 or anti-Rhesus D antibodies according to one of the claims 10 to 12.

Abstract

Polypeptides capable of forming antigen binding structures specific for Rhesus D antigens include the sequences indicated in the figs. 1a to 17 b. They are prepared in a process comprising the following steps in sequential order:

- boosting of an individual capable of forming anti-Rhesus D antibodies with Rhesus D positive red blood cells,
- isolating mononuclear cells from the individual,
- isolating total RNA from the mononuclear cells,
- preparing a cDNA by using an oligo(dT)primer and reverse transcribing of the mRNA with M-MuLV reverse transcriptase and amplifying the cDNA repertoire by a polymerase chain reaction using immunoglobulin gene family specific primers,
- creating a phage display library by inserting the DNA coding for the heavy and light chain of the Fab polypeptide into a phagemid vector; the DNA for the heavy chain is inserted in frame into the gene coding for the phage protein pIII which allows the expression of a Fab pIII fusion protein on the surface of the phage,
- transforming bacterial cells with the obtained recombinant plasmids, cultivation of the transformed bacterial cells and co-expression of the heavy and the light chain of a Fab on filamentous phage particles,
- amplifying the Fab-carrying phage in bacteria,
- selecting individual phage clones by several rounds of panning on Rhesus positive red blood cells,
- isolating the plasmid DNA from the selected clones and cutting out the gIII gene,
- transforming bacterial cells with the obtained plasmid, cultivating of the transformed bacterial cells expressing the Fab, and isolating the Fab fragments.

The obtained polypeptides, being Fab fragments, can be used directly as an active ingredient in pharmaceutical and diagnostic compositions. The Fab and their DNA sequences can also be used for the preparation of complete recombinant Anti-Rhesus D antibodies.

(1) GENERAL INFORMATION

(i) APPLICANT:
(A) NAME: Rotkreuzstiftung Zentrallaboratorium Blutspendedienst SRK
(B) STREET: Wankdorfstrasse 10
(C) CITY: Bern 22
(D) STATE OR PROVINCE:
(E) COUNTRY: Switzerland
(F) POSTAL CODE: CH-3000

(ii) TITLE OF INVENTION: Polypeptides capable of forming antigen binding structures with specificity for the Rhesus D antigens, the DNA encoding them and the process for their preparation and use

(iii) NUMBER OF SEQUENCES: 34
(iv) COMPUTER-READABLE FORM:
(A) MEDIUM TYPE: 3.5" Floppy disk, 1.44 MB
(B) COMPUTER: IBM compatible PC
(C) OPERATING SYSTEM: IBM-DOS 6.3/Windows 3.1
(D) SOFTWARE: MS Word for Windows 6.0 /saved as MS-DOS text

(v) CURRENT APPLICATION DATA: n.a.
(A) APPLICATION NUMBER: n.a.

6

(2) INFORMATION FOR SEQ ID NO: 1 (LD1-28-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-28
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 1 (LD1-28-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG      48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                  5                  10                  15

TCC CTG AGA CTC TCC TGT GAA GCG TCT GGA TTC GCC CTC AGA AGT TCT      96
Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Ala Leu Arg Ser Ser
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCT GGC AAG GGG ATG GAG TGG GTG     144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Met Glu Typ Val
        35                  40                  45

GCA CTT ATA TGG TTT GAT GGA AGT ATC AGA TCG TAT GCA GAA TCC GCG     192
Ala Leu Ile Typ Phe Asp Gly Ser Ile Arg Ser Tyr Ala Glu Ser Ala
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC ACT TCC AAG AAC ACC CTA TAT     240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTC CAT ATG CGC AGT CTG AGT GCC GAC GAC ACG GAT GTG TTT TAC TGT     288
Leu His Met Arg Ser Leu Ser Ala Asp Asp Thr Asp Val Phe Tyr Cys
                85                  90                  95

GCG AGA GAC AAG GCG GTT CGG GGA ATT AAC AGG TAC AAC TAT TAC ATG     336
Ala Arg Asp Lys Ala Val Arg Gly Ile Asn Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GTC AAA GGG ACC ACG GTC ACC GTC TCC TCA                 375
Asp Val Typ Val Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO:2 (LD1-28-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 318 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-28
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..288)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 2 (LD1-28-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA    48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                5                   10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AAC ATT ATC CGC TAT TTA AAT    96
Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Ile Arg Tyr Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAG CCA GGG AAA GCC CCT AGG CTC CTG ATC TAT GGT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile Tyr Gly
        35                  40                  45

GCG TCC ACT TTG CAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA   192
Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGT AGT CTG CAA CCT GAA GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA CAG AGT TAC CGT ACC CCT CCA TTC ACT   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Pro Phe Thr
                85                  90                  95

TTC GGC CCT GGG ACC AAA GTG GAG ATC AAA                          318
Phe Gly Pro Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 3 (LD1-40-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-40
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q 32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 3 (LD1-40-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
                5                   10                  15

TCC CTG AGA CTC TCC TGT ATA GCG TCT GGA TTC ACC CTC AGG AAT TAT     96
Ser Leu Arg Leu Ser Cys Ile Ala Ser Gly Phe Thr Leu Arg Asn Tyr
            20                  25                  30

GCC ATG CAC TGG GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG    144
Ala Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCA GGT ATA TGG TTT GAT GGA AGT AAC AAA AAC TAT GCA GAC TCC GTG    192
Ala Gly Ile Typ Phe Asp Gly Ser Asn Lys Asn Tyr Ala Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC AAT TCC AAG AAC ACG CTG TTT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80

CTG CAA CTG AAC AGC CTG AGA GAC GAG GAC ACG GCT GTG TAT TAT TGT    288
Leu Gln Leu Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG CGA GCA GCA CGT GGT ATT TCT AGG TTC TAT TAC TAC ATG    336
Ala Arg Glu Arg Ala Ala Arg Gly Ile Ser Arg Phe Tyr Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC CCA                375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Pro
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 4 (LD1-40-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 318 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-40
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: 2p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..288)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO.4 (LD1-40-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGC GAC AGA    48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AGC ATT AGG AGC CAT TTG AAT    96
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Ser His Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGG AAA GCC CCT AAG TTG CTG ATC TAT GGT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly
        35                  40                  45

GCG TCC ACT TTG CAA AGT GGC GTC CCA TCA AGG TTC AGT GGC AGT GGC   192
Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG GCA GTT TTC ACT CTC ACC ATC GCC AGT CTA CAA CCT GAA GAT   240
Ser Gly Ala Val Phe Thr Leu Thr Ile Ala Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA GAG AGT TAC AGT AAT CCT CTA ATC ACC   288
Phe Ala Thr Tyr Tyr Cys Gln Glu Ser Tyr Ser Asn Pro Leu Ile Thr
                85                  90                  95

TTC GGC CAA GGG ACA CGA CTG GAG ACT AAA                          318
Phe Gly Gln Gly Thr Arg Leu Glu Thr Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 5 (LD1-52-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-52
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO.5 (LD1-52-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                 5                  10                  15

TCC CTG AGA CTC TCC TGT GAA GCG TCT GGA TTC GCC CTC AGA AGT TCT     96
Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Ala Leu Arg Ser Ser
            20                  25                  30

GGA ATG CAC TGG GTC CGC CAG GCT CCT GGC AAG GGG CTG GAG TGG GTG    144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCA CTT ATA TGG TTT GAT GGA AGT ATC AGA TCG TAT GCA GAA TCC GTG    192
Ala Leu Ile Typ Phe Asp Gly Ser Ile Arg Ser Tyr Ala Glu Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC ACT TCC AAG AAC ACC CTA TAT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTC CAA ATG CGC AGT CTG AGT GCC GAC GAC ACG GCT GTG TAT TAC TGT    288
Leu Gln Met Arg Ser Leu Ser Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAC AAG GCG GTT CGG GGA ATT AGC AGG TAC AAC TAT TAC ATG    336
Ala Arg Asp Lys Ala Val Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA                375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 6 (LD1-52-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 318 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-52
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..288)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO.6 (LD1-52-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AAC ATT ATC CGC TAT TTA AAT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Ile Arg Tyr Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAG CCA GGG AAA GCC CCT AGG CTC CTG ATC TAT GGT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile Tyr Gly
        35                  40                  45

GCG TCC ACT TTG CAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA   192
Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGT AGT CTG CAA CCT GAA GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA CAG AGT TAC CGT ACC CCT CCA TTC ACT   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Pro Phe Thr
                85                  90                  95

TTC GGC CCT GGG ACC AAA GTG GAG ATC AAA                          318
Phe Gly Pro Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO:7 (LD1-84-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-84
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION:q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO.7 (LD1-84-VH)

```
CAG GTA AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                  5                  10                  15

TCC CTG AGA CTC TCC TGT GAA GCG TCT GGA TTC ACC CTC AGA AGT TCT     96
Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Thr Leu Arg Ser Ser
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCT GGC AAG GGG CTG GAG TGG GTG    144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

ACA CTT ATA TGG TTT GAT GGA AGT ATC AGA TCG TAT GCA GAA TCC GTG    192
Thr Leu Ile Typ Phe Asp Gly Ser Ile Arg Ser Tyr Ala Glu Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC ACT TCC AAG AAC ACC CTA TAT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTC CAA ATG CGC AGT CTG AGT GCC GAC GAC ACG GCT GTG TAT TAC TGT    288
Leu Gln Met Arg Ser Leu Ser Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAC AAG GCG GTT CGG GGA ATT AGC AGG TAC AAC TAT TAC ATG    336
Ala Arg Asp Lys Ala Val Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA                375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 8 (LD1-84-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-84
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..285)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 8 (LD1-84-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT ATA GGA Phe Thr   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Ile Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACC TGC CGG GCA AGT CAG AGT ATC ATC AGG TAT TTG AAT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ile Arg Tyr Leu Asn
            20                  25                  30

TGG TAT CAG CAC AAA CCA GGA AAA GCC CCT AAA CTC CTC ATC TTT GCT   144
Typ Tyr Gln His Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Phe Ala
        35                  40                  45

GCA TCG AAT TTG CAA ACT GGG GTC CCA TCC AGG TTC AGT GGC AGT GGA   192
Ala Ser Asn Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGT GAC CTG CAG CCT GAG GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asp Leu Gln Pro Glu Asp
65                  70                  75                  80

TTC GCA ACT TAC TAC TGT CAA CAG AGT TAC AGT AGG CCG TTC ACT TTT   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Arg Pro Phe Thr Phe
                85                  90                  95

GGC CGG GGG ACC AGC CTG GAC ATC AAA                              315
Gly Arg Gly Thr Ser Leu Asp Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 9 (LD1-98-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-98
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 9 (LD1-98-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                  5                  10                  15

TCC CTG AGA CTC TCC TGT GAA GCG TCT GGA TTC GCC CTC AGA AGT TCT     96
Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Ala Leu Arg Ser Ser
            20                  25                  30

GAC ATA CAC TGG GTC CGC CAG GCT CCT GGC AAG GGG CTG GAG TGG GTG    144
Asp Ile His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCA CTT ATA TGG TTT GAT GGA AGT ATC AGA TCG TAT GCA GAA TCC GTG    192
Ala Leu Ile Typ Phe Asp Gly Ser Ile Arg Ser Tyr Ala Glu Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC ACT TCC AAG AAC ACC CTA TAT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTC CAA ATG CGC AGT CTG AGT GCC GAC GAC ACG CGT GTG TAT TAC TGT    288
Leu Gln Met Arg Ser Leu Ser Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAC AAG GCG GTT CGG GGA ATT AGC AGG TAC AAC TAT TAC ATG    336
Ala Arg Asp Lys Ala Val Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA                375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 10 (LD1-98-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 318 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-98
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..288)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 10 (LD1-98-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA    48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AAC ATT ATC CGC TAT TTA AAT    96
Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Ile Arg Tyr Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAG CCA GGG AAA GCC CCT AGG CTC CTG ATC TAT GGT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile Tyr Gly
        35                  40                  45

GCG TCC ACT TTG CAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA   192
Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGT AGT CTG CAA CCT GAA GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA CAG AGT TAC CGT ACC CCT CCA TTC ACT   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Thr Pro Pro Phe Thr
                85                  90                  95

TTC GGC CCT GGG ACC AAA GTG GAG ATC AAA                          318
Phe Gly Pro Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 11 (LD1-110-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-110
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 11 (LD1-110-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
                 5                  10                  15

TCC CTG AGA CTC TCC TGT ATA GCG TCT GGA TTC ACC CTC AGG AAT TAT     96
Ser Leu Arg Leu Ser Cys Ile Ala Ser Gly Phe Thr Leu Arg Asn Tyr
            20                  25                  30

GCC ATG CAC TGG GTC CGC CAG GCT CCA GGA AAG GGG CTG GAG TGG GTG    144
Ala Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCA GGT ATA TGG TTT GAT GGA AGC AAC AAA AAC TAT GCA GAC TCC GTG    192
Ala Gly Ile Typ Phe Asp Gly Ser Asn Lys Asn Tyr Ala Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC AAC TCC AAG AAC ACT CTG TTT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80

CTG CAC ATG AAC AGC CTG AGA GCC GAG GAC ACG GCT ACA TAT TAC TGT    288
Leu His Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Thr Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG AGG GCG ATT CGG GGA ATC AGT AGA TAC AAT TAC TAC ATG    336
Ala Arg Glu Arg Ala Ile Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAG GGG ACC ACG GTC ACC GTC TCC TCA                375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 12 (LD1-110-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-110
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..285)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 12 (LD1-110-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA    48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AGC ATT CGA AGC TCT TTA AAT    96
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Ser Ser Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGG AAA GCC CCT AAA GTC CTG ATC TAT GCT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile Tyr Ala
        35                  40                  45

GCA TCC AGT TTG CAA AGT GGG GTC CCA TCC AGG TTC AGT GGC AGA GGA   192
Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Arg Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGC AGT CTG CAG CCT GAA GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCG ACT TAT TAT TGT CAA CAG AGT TCC AGT TCC TCG TGG ACG TTC   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Ser Ser Ser Typ Thr Phe
                85                  90                  95

GGC CAA GGG ACC AAG GTG GAA ATC AAA                              315
Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 13 (LD1-117-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 378 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-117
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..345)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 13 (LD1-117-VH)

```
CAG GTG AAA CTG CTC GAG TCA GGA GGA GGC GTG GTC CAG CCT GGG AAG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
                  5                  10                  15

TCC CTG AGA CTT TCC TGT GCA GCG TCT GGA TTC AGT TTC AAT AGC CAT     96
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Asn Ser His
            20                  25                  30

GGN ATG CAC TGG GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG    144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCA TTT ATT TGG TTT GAT GGC AGT AAT AAA TAC TAT GCA GAC TCC GTG    192
Ala Phe Ile Typ Phe Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60

AAG GGC CGT TTC ACC ATC ACC AGA GAC AAC TCC AAG AAC ACG CTG TAT    240
Lys Gly Arg Phe Thr Ile Thr Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTN CAA ATG AAC AGC CTG AGA GCC GAG GAC ACG GCT GTC TAT TAC TGT    288
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG ACC TCA GTA AGG CTA GGG TAT AGC CGC TAC AAT TAC TAC    336
Ala Arg Glu Thr Ser Val Arg Leu Gly Tyr Ser Arg Tyr Asn Tyr Tyr
            100                 105                 110

ATG GAC GTC TGG GCC AAA GGG ACC ACG GTC ACC ATC TCG TCA            378
Met Asp Val Typ Ala Lys Gly Thr Thr Val Thr Ile Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 14 (LD1-117-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 318 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-117
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..288)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 14 (LD1-117 VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AGC ATT AGG AGC CAT TTG AAT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Ser His Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGG AAA GCC CCT AAG CTC CTG ATC TAT GCT  144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
        35                  40                  45

GCA TCC AGT TTG CAA GGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA  192
Ala Ser Ser Leu Gln Gly Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGC AGT CTG CAA CCT GAA GAT  240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAT TAC TGT CAA CAG AGT TAC AGG GCC CCT CAG TGG ACG  288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Arg Ala Pro Gln Typ Thr
                85                  90                  95

TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA                         318
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 15 (LD2-1-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-1
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 15 (LD2-1-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG    48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                5                  10                  15

TCC CTG AGA CTC TCC TGT GTA GCG TCT GGA TTC ACC CTC AGG AGT TAT    96
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Leu Arg Ser Tyr
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCA GGA AAG GGC CTG GAG TGG GTG   144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCT TTT ATA TGG TTT GAT GGA AGT AAT AAA GGA TAT GTA GAC TCC GTG   192
Ala Phe Ile Typ Phe Asp Gly Ser Asn Lys Gly Tyr Val Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC CGA GAC AAT TCC AAG AAC ATG GTC TAT   240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Met Val Tyr
65                  70                  75                  80

CTC CAA ATG AAC AGC CTG AGA GCC GAT GAC ACG GCT GTA TAT TAT TGT   288
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG AAG GCG CTT CGG GGA ATC AGC AGA TAC AAC TAT TAC CTG   336
Ala Arg Glu Lys Ala Leu Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Leu
            100                 105                 110

GAC GTC TGG GGC AAG GGG ACC ACG GTC ACC GTC TCC TCA               375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 16 (LD2-1-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 333 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-1
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 22
(B) MAP POSITION: q11.2
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (61..99, 145..165 , 262..294)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 16 (LD2-1-VL)

```
GTG GTG ACT CAG CCA CCC TCA GCG TCT GGG ACC CCC GGA CAG AGG GTC   48
Val Val Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val
                 5                  10                  15

ACC ATC TCT TGT TCT GGA AGC AAC TCC ATC CTT GGA AGT AAG TAT GTA   96
Thr Ile Ser Cys Ser Gly Ser Asn Ser Ile Leu Gly Ser Lys Tyr Val
            20                  25                  30

TAC TGG TAC CAG AAA CTC CCA GGA ACG GCC CCC AAA CTC CTC ATC TAT   144
Tyr Typ Tyr Gln Lys Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr
        35                  40                  45

AAG AAT GAT CAG CGG CCC TCA GGG GTC TCT GAC CGA TTC TCT GGC TCC   192
Lys Asn Asp Gln Arg Pro Ser Gly Val Ser Asp Arg Phe Ser Gly Ser
    50                  55                  60

AAG TCT GGC ACC TCG GCC TCC CTG GCC ATC AGT GGG CTC CGG TCC GAG   240
Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Glu
65                  70                  75                  80

GAT GAG GCT GAC TAT TAC TGT GCA CCA TGG GAT GCC AAC CTG GGT GGC   288
Asp Glu Ala Asp Tyr Tyr Cys Ala Pro Typ Asp Ala Asn Leu Gly Gly
                85                  90                  95

CCG GTG TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA AGT CAG CCC       333
Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Ser Gln Pro
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO: 17 (LD2-4-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-4
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 17 (LD2-4-VH)

```
CAG GTG AAA CTG CTC GAG TCG GGG GGA GGC GTG GTC CAG CCG GGG GGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                  5                  10                  15

TCC CTG AGA CTC TCC TGT GAA GCG TCT GGA TTC ACC CTC AGA AGT TCT     96
Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Thr Leu Arg Ser Ser
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCT GGC AAG GGG CTG GAG TGG GTG    144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCA CTT ATA TGG TTT GAT GGA AGT ATC AGA TCG TAT GCA GAA TCC GTG    192
Ala Leu Ile Typ Phe Asp Gly Ser Ile Arg Ser Tyr Ala Glu Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC ACT TCC AAG AAC ACC CTA TAT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTC CAA ATG CGC AGT CTG AGT GCC GAC GAC ACG GCT GTG TAT TAC TGT    288
Leu Gln Met Arg Ser Leu Ser Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAC AAG GCG GTT CGG GGA ATT AGC AGG TAC AAC TAT TAC ATG    336
Ala Arg Asp Lys Ala Val Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA                375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 18 (LD2-4-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 312 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-4
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..282)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 18 (LD2-4-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG ACA AGT CAG ACC ATT AGC AGA AAT TTA CAT   96
Val Thr Ile Thr Cys Arg Thr Ser Gln Thr Ile Ser Arg Asn Leu His
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGG AAA GCC CCT AAG CTC CTG ATC TAT GCT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
        35                  40                  45

ACA TCC AGT TTG CAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA   192
Thr Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50      --          55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AAT AGT CTA CAA CCT GAA GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA CAG AGT TAC ACT ACC CCT TCG TTC GGC   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Thr Thr Pro Ser Phe Gly
                85                  90                  95

CAA GGG ACC AAG GTG GAA ATC AAA                                  312
Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 19 (LD2-5-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-5
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 19 (LD2-5-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC TTG GTC CAG CCG GGG GGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                  5                  10                  15

TCC CTG AGA CTC TCC TGT GTA GCG TCT GGA TTC ACC TTC AGG AGT TAT     96
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20                  25                  30

GGA ATG CAC TGG GTC CGC CAG GCT CCA GGA AAG GGC CTG GAG TGG GTG    144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCT TTT ATA TGG TTT GAT GGA AGT AAT AAA GGA TAT GTA GAC TCC GTG    192
Ala Phe Ile Typ Phe Asp Gly Ser Asn Lys Gly Tyr Val Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC CGA GAC AAT TCC AAG AAC ATG CTC TAT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Met Leu Tyr
65                  70                  75                  80

CTG CAA ATG AAT AGC CTG AGA GCC GAG GAC ACG GCT GTA TAT TAT TGT    288
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG AAG GCG CTT CGG GGA ATC AGT AGA TAC AAC TAT TAC CTG    336
Ala Arg Glu Lys Ala Leu Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Leu
            100                 105                 110

GAC GTC TGG GGC AAG GGG GCC ACG GTC ACC GTC TCC TCA                375
Asp Val Typ Gly Lys Gly Ala Thr Val Thr Val Ser Ser
        115                 120                 125
```

22) INFORMATION FOR SEQ ID NO: 20 (LD2-5-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 318 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-5
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..288)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 20 (LD2-5-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GTA TCT ATA GGC GAC AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ile Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AGC GTT ACC AGG TCT TTA AAT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Thr Arg Ser Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGG AAA GCC CCT AGG CTC CTA ATC TTT GGT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile Phe Gly
        35                  40                  45

GCG TCC ACT TTG CAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA   192
Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACC CTC ACC ATC AGC AGT CTG CAA CCT GAG GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GGA ACT TAC TAC TGT CAA CAG AAT TAC AGG ACC CCT CAG TGG ACG   288
Phe Gly Thr Tyr Tyr Cys Gln Gln Asn Tyr Arg Thr Pro Gln Typ Thr
                85                  90                  95

TTC GGC CAA GGG ACC AAG GTA GAA ATC AAA                          318
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 21 (LD2-10-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 378 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-10
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 298..345)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 21 (LD2-10-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG    48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                 5                  10                  15

TCC CTG AGA CTC TCC TGT GTA GCG TCT GGA TTC ACC CTC AGG AGT TAT    96
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Leu Arg Ser Tyr
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCA GGC AAG GGC CTG GAG TGG GTG   144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCT TTT ATA TGG TTT GAT GGA AGT AAT AAA GGA TAT GTA GAC TCC GTG   192
Ala Phe Ile Typ Phe Asp Gly Ser Asn Lys Gly Tyr Val Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC CGA GAC AAT TCC AAG AAC ATG GTC TAT   240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Met Val Tyr
65                  70                  75                  80

CTG CAA ATG AAC AGC CTG AGA GCC GAT GAC ACG GCT GTA TAT TAT TAT   288
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Val Tyr Tyr Tyr
                85                  90                  95

TGT GCG AGA GAG AAG GCG CTT CGG GGA ATC AGC AGA TAC AAC TAT TAC   336
Cys Ala Arg Glu Lys Ala Leu Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr
            100                 105                 110

CTG GAC GTC TGG GGC AAG GGG ACC ACG GTC ACC GTC TCC TCA           378
Leu Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 22 (LD2-10-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 333 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-10
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 22
(B) MAP POSITION: q11.2
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (61..102, 148..168, 265..294)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 22 (LD2-10-VL)

```
GTG GTG ACT CAG GAG CCC TCA CTG ACT GTG TCC CCA GGA GGG ACA GTC   48
Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val
                 5                  10                  15

ACT CTC ACC TGT GCT TCC AGC ACT GGG GCA GTC ACC AGG GGT TAC TAT   96
Thr Leu Thr Cys Ala Ser Ser Thr Gly Ala Val Thr Arg Gly Tyr Tyr
            20                  25                  30

CCA AAC TGG TTC CAG CAG AAG CCT GGA CAA GCA CCC AGG GCA CTG ATT   144
Pro Asn Typ Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Ala Leu Ile
        35                  40                  45

TAT AGT ACA AAC AAA AAA CAC TCC TGG ACC CCT GCC CGG TTC TCA GGC   192
Tyr Ser Thr Asn Lys Lys His Ser Typ Thr Pro Ala Arg Phe Ser Gly
    50                  55                  60

TCC CTC CTT GGG GGC AAA GCT GCC CTG ACA CTG TCA GGT GTG CAG CCT   240
Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro
65                  70                  75                  80

GAA GAC GAG GCT GAA TAT TAC TGC CTG CTC TAC TAT GGT GGT GCT CAA   288
Glu Asp Glu Ala Glu Tyr Tyr Cys Leu Leu Tyr Tyr Gly Gly Ala Gln
                85                  90                  95

CTC GTA TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA CGT CAG CCC       333
Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Arg Gln Pro
            100                 105                 110
```

(2) INFORMATION FOR SEQ ID NO: 23 (LD2-11-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-11
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 23 (LD2-11-VH)

```
CAG GTG AAA CTG CTC GAG TCG GGG GGA GGC GTG GTC CAG CCG GGG GGG    48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                  5                  10                  15

TCC CTG AGA CTC TCC TGT GAA GCG TCT GGA TTC ACC CTC AGA AGT TCT    96
Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Thr Leu Arg Ser Ser
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCT GGC AAG GGG CTG GAG TGG GTG   144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCA CTT ATA TGG TTT GAT GGA AGT ATC AGA TCG TAT GCA GAA TCC GTG   192
Ala Leu Ile Typ Phe Asp Gly Ser Ile Arg Ser Tyr Ala Glu Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC ACT TCC AAG AAC ACC CTA TAT   240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Thr Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTC CAA ATG CGC AGT CTG AGT GCC GAC GAC ACG GCT GTG TAT TAC TGT   288
Leu Gln Met Arg Ser Leu Ser Ala Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAC AAG GCG GTT CGG GGA ATT AGC AGG TAC AAC TAT TAC ATG   336
Ala Arg Asp Lys Ala Val Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA               375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 24 (LD2-11-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-11
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..285)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 24 (LD2-11-VL)

```
GTG TTG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT ATA CGA GAC AGA   48
Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Ile Arg Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AAC ATT GGC AGT TAT TTA AAT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Gly Ser Tyr Leu Asn
            20                  25                  30

TGG TAT CAG CAC AAA CCA GGG ACA GCC CCT AAA CTC CTG ATC TAT GCT   144
Typ Tyr Gln His Lys Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Ala
        35                  40                  45

GTA TCC GCT TTG CAA AGT GGG GTC CCA TCG AGG TTC AGT GGC AGT AGA   192
Val Ser Ala Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
    50              55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGC AGT CTG CAA CCT GAA GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA CAG AGT TAC AGT CCC CCG TAC ACT TTC   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Pro Pro Tyr Thr Phe
                85                  90                  95

GGG CAG GGG ACC AAC CTG CAG ATC AAA                              315
Gly Gln Gly Thr Asn Leu Gln Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 25 (LD2-14-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-14
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 25 (LD2-14-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG    48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                 5                  10                  15

TCC CTG AGA GTC GCC TGT GTA GCG TCT GGA TTC ACC TCC AGG AAT TTT    96
Ser Leu Arg Val Ala Cys Val Ala Ser Gly Phe Thr Ser Arg Asn Phe
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCA GGA AAG GGG CTG GAG TGG GTG   144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GTT TTT ATT TGG TTT GAT GCA AGT AAT AAA GGA TAT GGA GAC TCC GTT   192
Val Phe Ile Typ Phe Asp Ala Ser Asn Lys Gly Tyr Gly Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC GTC TCC AGA GAC AAT TCC AAG AAC ACG CTC TAT   240
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTG CAA ATG AAC GGC CTG AGA GCC GAA GAC ACG GCT GTA TAT TAT TGT   288
Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG AAG GCG GTT CGG GGA ATT AGT AGA TAC AAC TAC TAC ATG   336
Ala Arg Glu Lys Ala Val Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Met
            100                 105                 110

GAC GTC TGG GGC AAG GGG ACC ACG GTC ACC GTC TCC TCA               375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 26 (LD2-14-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-14
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..285)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 26 (LD2-14-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTG GGA GAC AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AGC ATT ATC AAC AAT TTA AAT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ile Asn Asn Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGC AAA GCC CCT GAA CTC CTG ATC TAT GCT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Glu Leu Leu Ile Tyr Ala
        35                  40                  45

GCA TCC AGT TTG CAA AGT GGG GTC CCT TCA AGG TTC CGT GGC AGT GGA   192
Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly Ser Gly
    50                  55                  60

TCT GGG AGA GAT TTC ACT CTC ACC GTC ACC AGT CTG CAA CCT GAA GAT   240
Ser Gly Arg Asp Phe Thr Leu Thr Val Thr Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA CAG AGT TAC AGT AAC CCT GTG GAC GTT   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Asn Pro Val Asp Val
                85                  90                  95

CGG CAA GGG ACC AAG GTG GAA ATC AAA                              315
Arg Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 27 (LD2-17-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-17
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 27 (LD2-17-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG    48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                 5                  10                  15

TCC CTG AGA CTC TCC TGT GTA GCG TCT GGA TTC ACC TCC AGG AGT TAT    96
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Ser Arg Ser Tyr
            20                  25                  30

GGA ATG CAC TGG GTC CGC CAG GCT CCA GGC AAG GGC CTG GAG TGG GTG   144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCT TTT ATA TGG TTT GAT GGA AGT AAT AAA GGA TAT GTA GAC TCC GTG   192
Ala Phe Ile Typ Phe Asp Gly Ser Asn Lys Gly Tyr Val Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC CGA GAC AAT TCC AAG AAC ACG CTC TAT   240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTG CAA ATG AAG AGC CTG AGA GCC GAG GAC ACG GCT GTA TAT TAT TGT   288
Leu Gln Met Lys Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG AAG GCG CTT CGG GGA ATC AGT AGA TAC AAC TAT TAC CTG   336
Ala Arg Glu Lys Ala Leu Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Leu
            100                 105                 110

GAC GTC TGG GGC AAG GGG ACC ACG GTC ACC GTC TCC TCA               375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 28 (LD2-17-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-17
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..285)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 28 (LD2-17-VL)

```
GTG ATG ACC CAG TCT CCA TTC TCC CTG TCT GCA TCT GTA GGA GAC AGA   48
Val Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AAC ATT AGG AGT TTT TTA AGT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Arg Ser Phe Leu Ser
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGG ACA GCC CCT AAG CTC CTG ATC TAT GCT  144
Typ Tyr Gln Gln Lys Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Ala
        35                  40                  45

GCA TCC AGG TTG CAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGG  192
Ala Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGC ACT CTG CAA CCT GAA GAT  240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Thr Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCG ACT TAC TAC TGT CAA CAG AGT TAC AGT GCC CCT TGG ACG TTC  288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ala Pro Typ Thr Phe
                85                  90                  95

GGC CAA GGG ACC AAG CTG GAA ATC AAA                             315
Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 29 (LD2-18-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-18
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 29 (LD2-18-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC TTG GTC CAG CCG GGG GGG    48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
                 5                  10                  15

TCC CTG AGA CTC TCC TGT GTA GCG TCT GGA TTC ACC TTC AGG AGT TAT    96
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Arg Ser Tyr
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCA GGC AAG GGC CTG GAG TGG GTG   144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCT TTT ATA TGG TTT GAT GGA AGT AAT AAA GGA TAT GTA GAC TCC GTG   192
Ala Phe Ile Typ Phe Asp Gly Ser Asn Lys Gly Tyr Val Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC CGA GAC AAT TCC AAG AAC ATG CTC TAT   240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Met Leu Tyr
65                  70                  75                  80

CTG CAA ATG AAT AGC CTG AGA GCC GAG GAC ACG GCT GTA TAT TAT TGT   288
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG AAG GCG CTT CGG GGA ATC AGT AGA TAC AAC TAT TAC CTG   336
Ala Arg Glu Lys Ala Leu Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Leu
            100                 105                 110

GAC GTC TGG GGC AAG GGG ACC ACG GTA ACC GTC TCC TCA               375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 30 (LD2-18-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 318 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-18
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..288)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 30 (LD2-18-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GTA TCT ATA GGG GAA AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ile Gly Glu Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GAA AGT CAG AGC GTT ACC AGG TCT TTA ATT   96
Val Thr Ile Thr Cys Arg Glu Ser Gln Ser Val Thr Arg Ser Leu Ile
            20                  25                  30

TGG TTT CAG AAG AAA CCA GGG AAA GCC CCT AGG CTC CTA ATC TTT GTT   144
Typ Phe Gln Lys Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile Phe Val
        35                  40                  45

GCG TCC ACT TGG AAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA   192
Ala Ser Thr Typ Lys Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACC CTC ACC ATC AGC AGT CTG CAA CCT GAG GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GGA ACT TAC TAC TGT CAA CAG AAT TAC AGG ACC CCT CAG TGG ACG   288
Phe Gly Thr Tyr Tyr Cys Gln Gln Asn Tyr Arg Thr Pro Gln Typ Thr
                85                  90                  95

TTC GGC CAA GGG ACC AAG GTA GAA ATC AAA                          318
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 31 (LD2-20-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 375 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-20
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..342)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 31 (LD2-20-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCG GGG GGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
                  5                  10                  15

TCC CTG AGA CTC TCC TGT GTA GCG TCT GGA TTC ACC TCC AGG AGT TAT     96
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Ser Arg Ser Tyr
            20                  25                  30

GGC ATG CAC TGG GTC CGC CAG GCT CCA GGA AAG GGC CTG GAG TGG GTG    144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

GCT TTT ATT TGG TTT GAT GGA AGT AAT AAA GGA TAT GTA GAC TCC GTG    192
Ala Phe Ile Typ Phe Asp Gly Ser Asn Lys Gly Tyr Val Asp Ser Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC CGA GAC AAT TCC AAG AAC ACG CTC TAT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

CTG CAA ATG AAG AGC CTG AGA GCC GAG GAC ACG GCT GTA TAT TAT TGT    288
Leu Gln Met Lys Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGA GAG AAG GCG CTT CGG GGA ATC AGT AGA TAC AAC TAT TAC CTG    336
Ala Arg Glu Lys Ala Leu Arg Gly Ile Ser Arg Tyr Asn Tyr Tyr Leu
            100                 105                 110

GAC GTC TGG GGC AAG GGG ACC ACG GTC ACC GTC TCC TCA                375
Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 32 (LD2-20-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD2
(B) CLONE: LD2-20
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: CHROMOSOME 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..285)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 32 (LD2-20-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                 5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG AGC ATT AGC AGC TAT TTA AAT   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
            20                  25                  30

TGG TAT CAG CAG AAA CCA GGG AAA GCC CCT AAG CTC CTG ATC TAT GCT   144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
        35                  40                  45

GCA TCC AGT TTG CAA AGT GGG GTC CCA TCA AGG TTC AGT GGC AGT GGA   192
Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGG ACA GAT TTC ACT CTC ACC ATC AGC AGT CTG CAA CCT GAA GAT   240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAC TAC TGT CAA CAG AGT TAC AGT ACC CGA TTC ACT TTC   288
Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Arg Phe Thr Phe
                85                  90                  95

GGC CCT GGG ACC AAA GTG GAT ATC AAA                              315
Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105
```

(2) INFORMATION FOR SEQ ID NO: 33 (LD1-6-17-VH)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 384 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-6-17
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 14
(B) MAP POSITION: q32.3
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (91..105, 148..198, 295..351)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 33 (LD1-6-17-VH)

```
CAG GTG AAA CTG CTC GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG     48
Gln Val Lys Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
                 5                  10                  15

TCC CTG AGA CTT TCC TGT GCA GCG TCT GGA TTT ACC TTC AGT AGC TAT     96
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

GGA ATG CAC TGG GTC CGC CAG GCT CCA GGA AAG GGG CTG GAG TGG GTG    144
Gly Met His Typ Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Typ Val
        35                  40                  45

ACA GAT ATA TGG TTT GAT GGA GGT AAT AAA CAT TAT GCA GAC TTC GTG    192
Thr Asp Ile Typ Phe Asp Gly Gly Asn Lys His Tyr Ala Asp Phe Val
    50                  55                  60

AAG GGC CGA TTC ACC ATC TCC AGA GAC AAT TCC AAG AAC ACG GGG TTT    240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Gly Phe
65                  70                  75                  80

CTA CAA ATG AAC AGC CTG AGA GTC GAG GAC ACG GCT GTG TAT TAC TGT    288
Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

GCG AGG GAT TAC TAT AGC GTT ACT AAG AAA CTC AGA CTC CAC TAC TAC    336
Ala Arg Asp Tyr Tyr Ser Val Thr Lys Lys Leu Arg Leu His Tyr Tyr
            100                 105                 110

TAC TAC ATG GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA    384
Tyr Tyr Met Asp Val Typ Gly Lys Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

(2) INFORMATION FOR SEQ ID NO: 34 (LD1-6-17-VL)
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 315 Base Pairs
(B) TYPE: Nucleic acid with corresponding protein
(C) STRANDEDNESS: Single
(D) TOPOLOGY: Linear
(ii) MOLECULE TYPE: cDNA to mRNA
(iii) HYPOTHETICAL: No
(iv) ANTI-SENSE: No
(vi) ORIGINAL SOURCE: N-terminal fragment
(A) ORGANISM: Homo sapiens
(B) STRAIN: Not applicable
(C) INDIVIDUAL / ISOLATE: Hyperimmune Rhesus D donor
(D) DEVELOPMENT STAGE: Adult, Rearranged development pattern
(E) HAPLOTYPE: Diploid
(F) TISSUE TYPE: Not applicable
(G) CELL TYPE: Peripheral lymphocyte B
(H) CELL LINE: Not applicable
(I) ORGANELLE: Not applicable
(vii) IMMEDIATE SOURCE: Escherichia coli
(A) LIBRARY: cDNA LIBRARY, LD1
(B) CLONE: LD1-6-17
(viii) POSITION IN GENOME:
(A) CHROMOSOME / SEGMENT: Chromosome 2
(B) MAP POSITION: p12
(C) UNITS: Chromosome band number
(xi) FEATURE:
(A) NAME / KEY: CDR1, CDR2, CDR3
(B) LOCATION: join base pair (64..96, 142..162, 259..285)
(C) IDENTIFICATION METHOD: By similarity with a known sequence
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO. 34 (LD1-6-17-VL)

```
GTG ATG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA   48
Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                5                  10                  15

GTC ACC ATC ACT TGC CGG GCA AGT CAG GGC ATT AGA AAT GAT TTA ACC   96
Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp Leu Thr
            20                  25                  30

TGG TAT CAG CAA AAA CCA GGG AAA GCC CCT AAG CTC CTG ATC TAT GCT  144
Typ Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
        35                  40                  45

GCA TCC AAT TTA CAA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA  192
Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    50                  55                  60

TCT GGC ACA GAT TTC ACT CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT  240
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65                  70                  75                  80

TTT GCA ACT TAT TAC TGT CTA CAA GAT AAC AAT TTC CCG TAC ACT TTT  288
Phe Ala Thr Tyr Tyr Cys Leu Gln Asp Asn Asn Phe Pro Tyr Thr Phe
                85                  90                  95

GGC CAG GGG ACC AAG CTG GAG ATC AAA                             315
Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

Fig. 1a

LD1-28-VH sequence

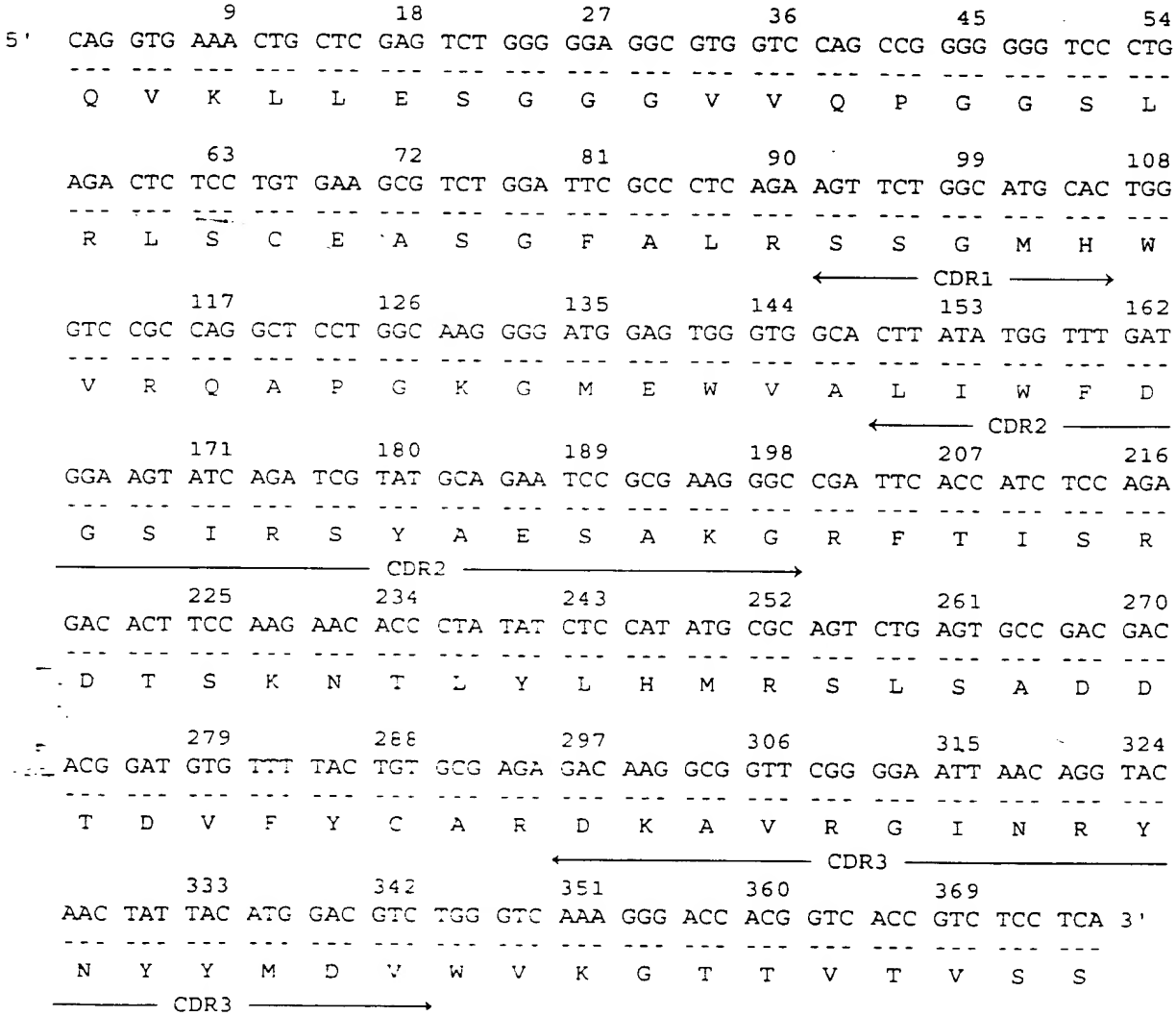


Fig. 1b

LD1-28-VL sequence

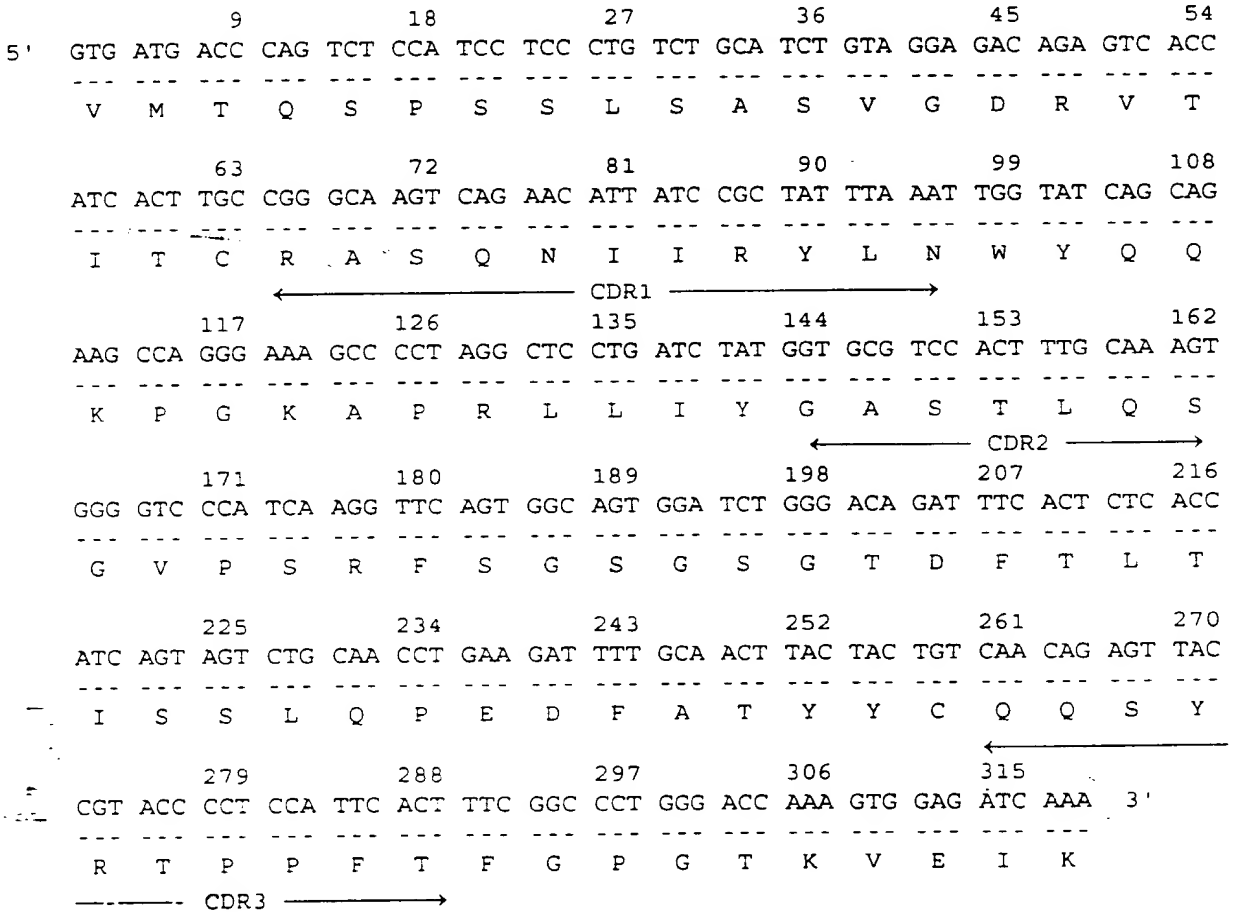


Fig. 2a

LD1-40-VH sequence

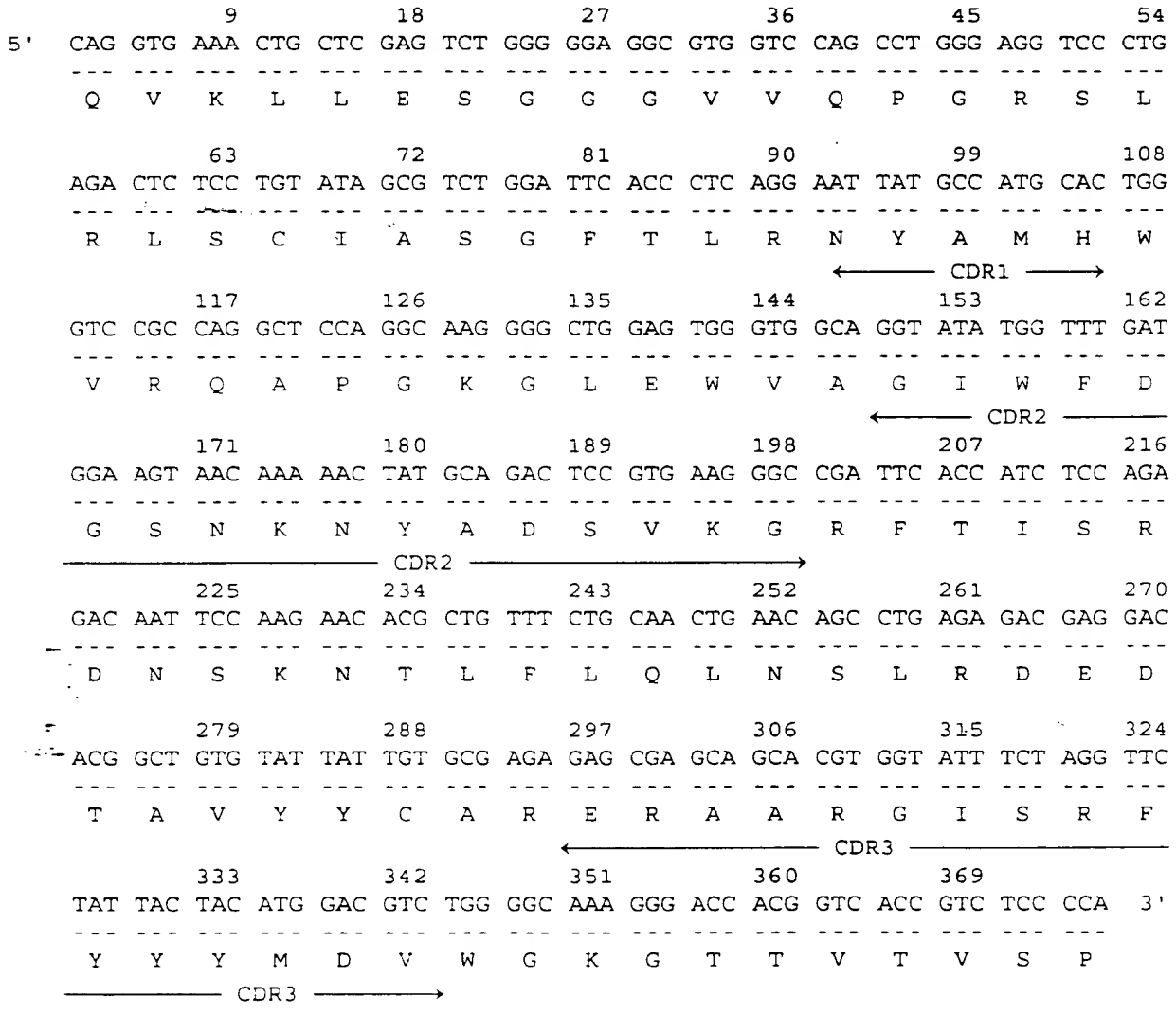


Fig. 2b

LD1-40-VL sequence

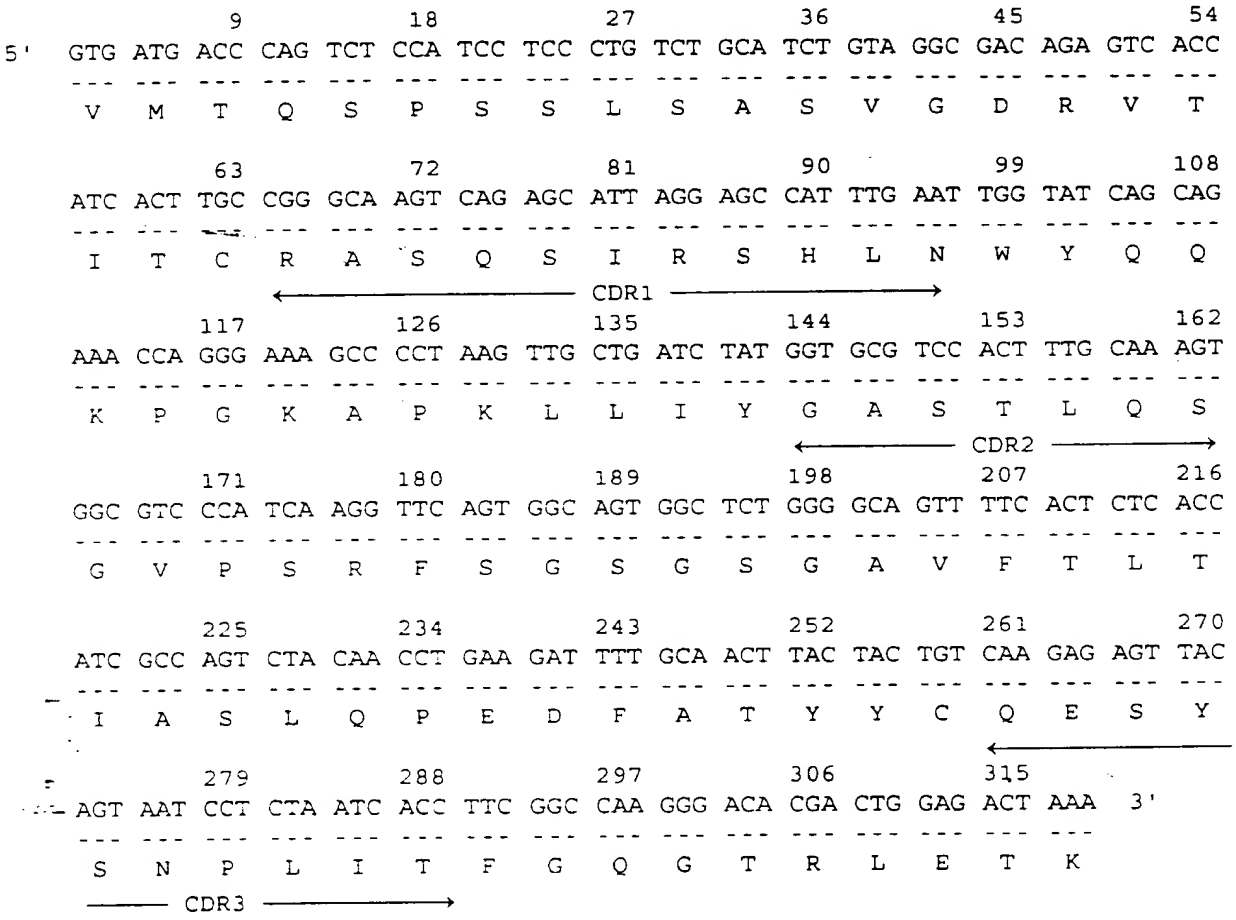


Fig. 3a

LD1-52-VH sequence

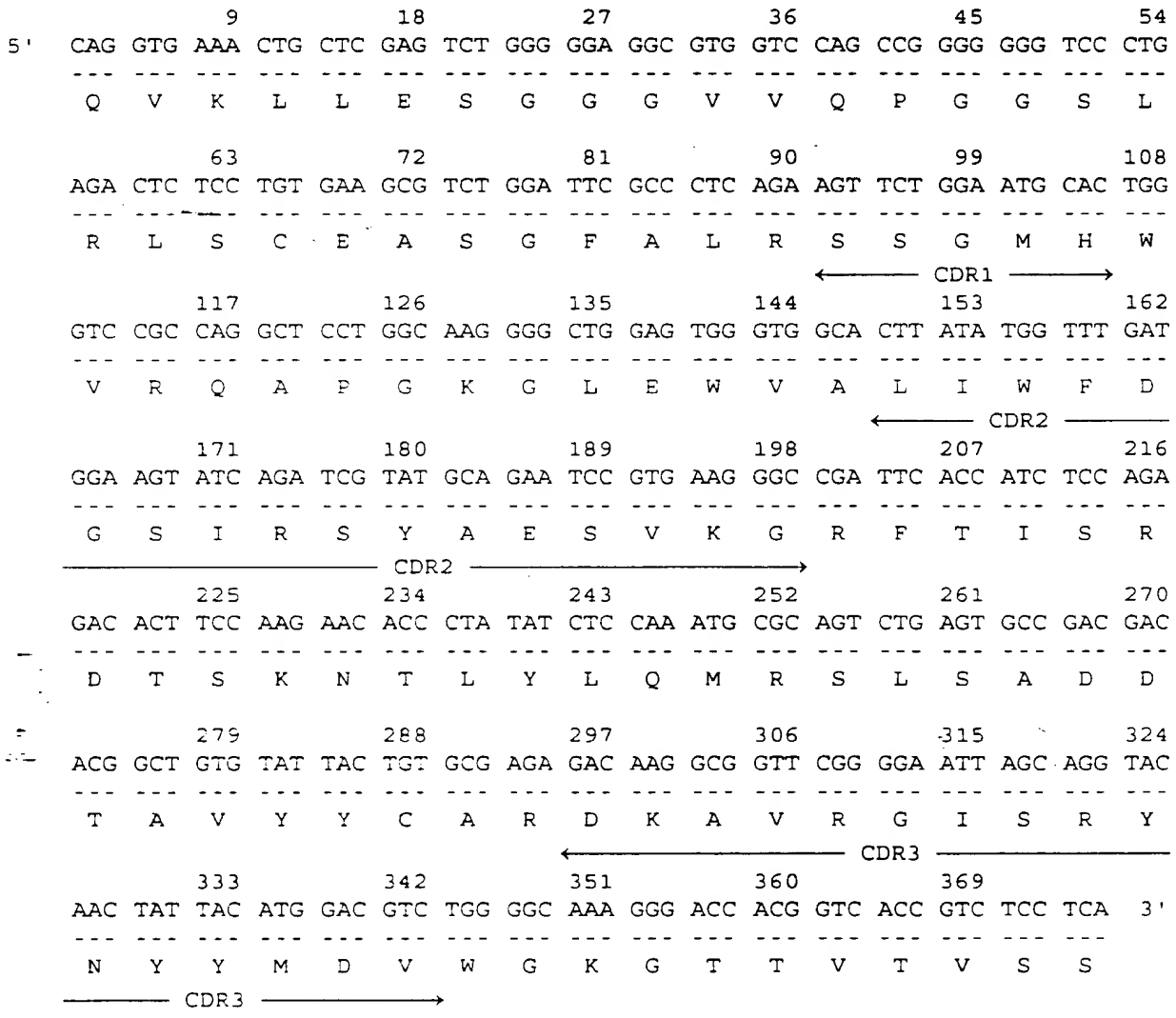


Fig. 3b

LD1-52-VL sequence

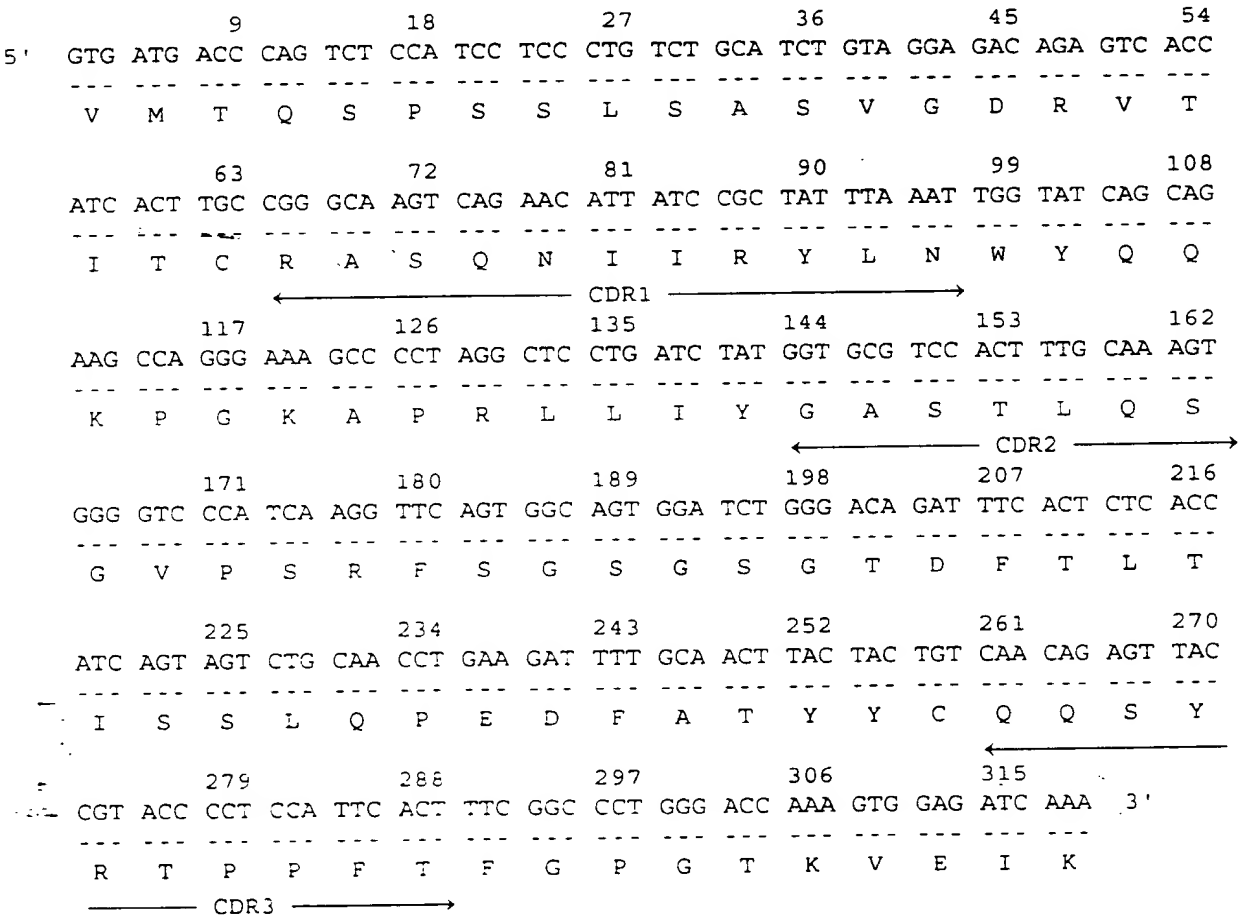


Fig. 4a

LD1-84-VH sequence

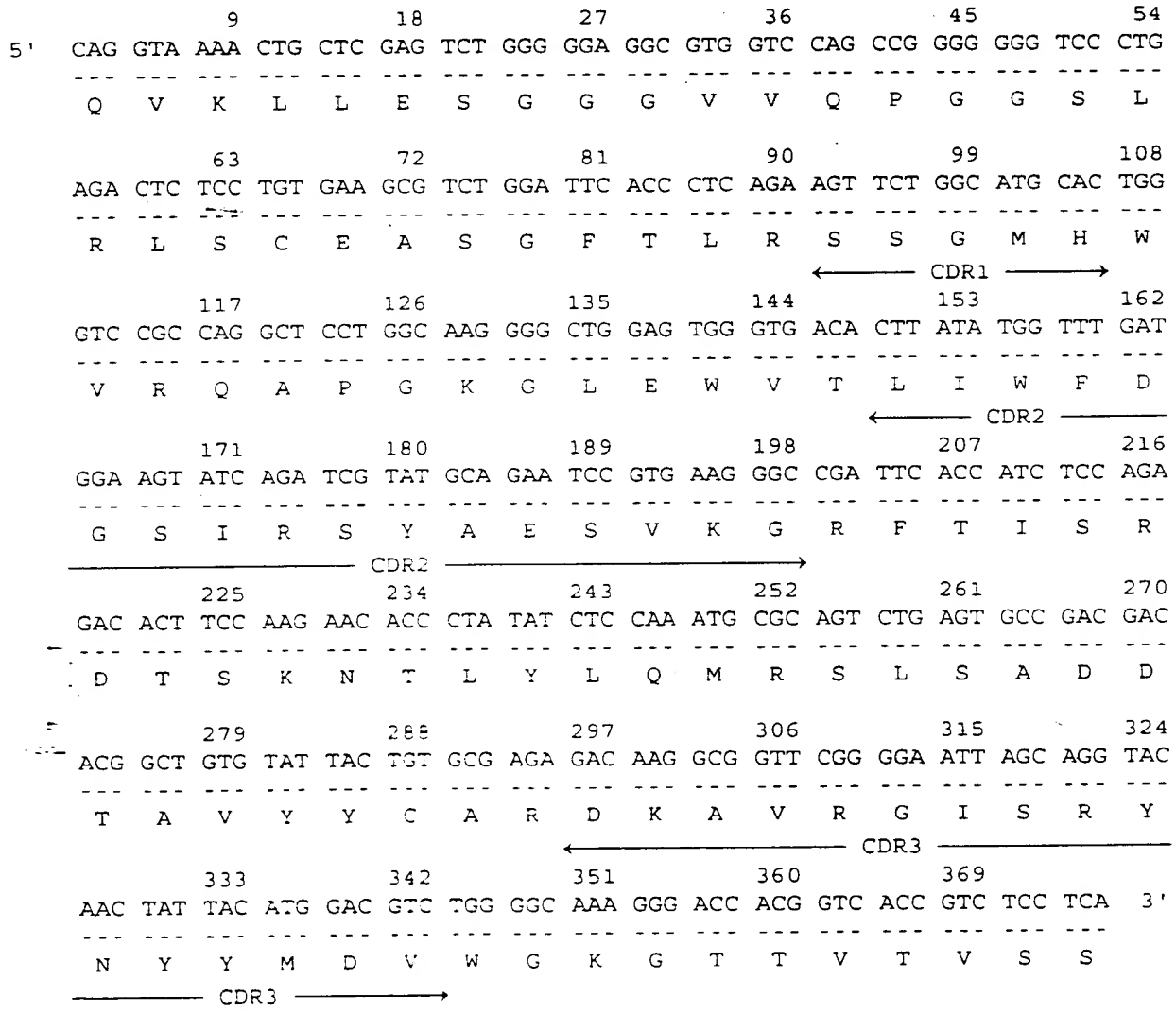


Fig. 4b

LD1-84-VL sequence

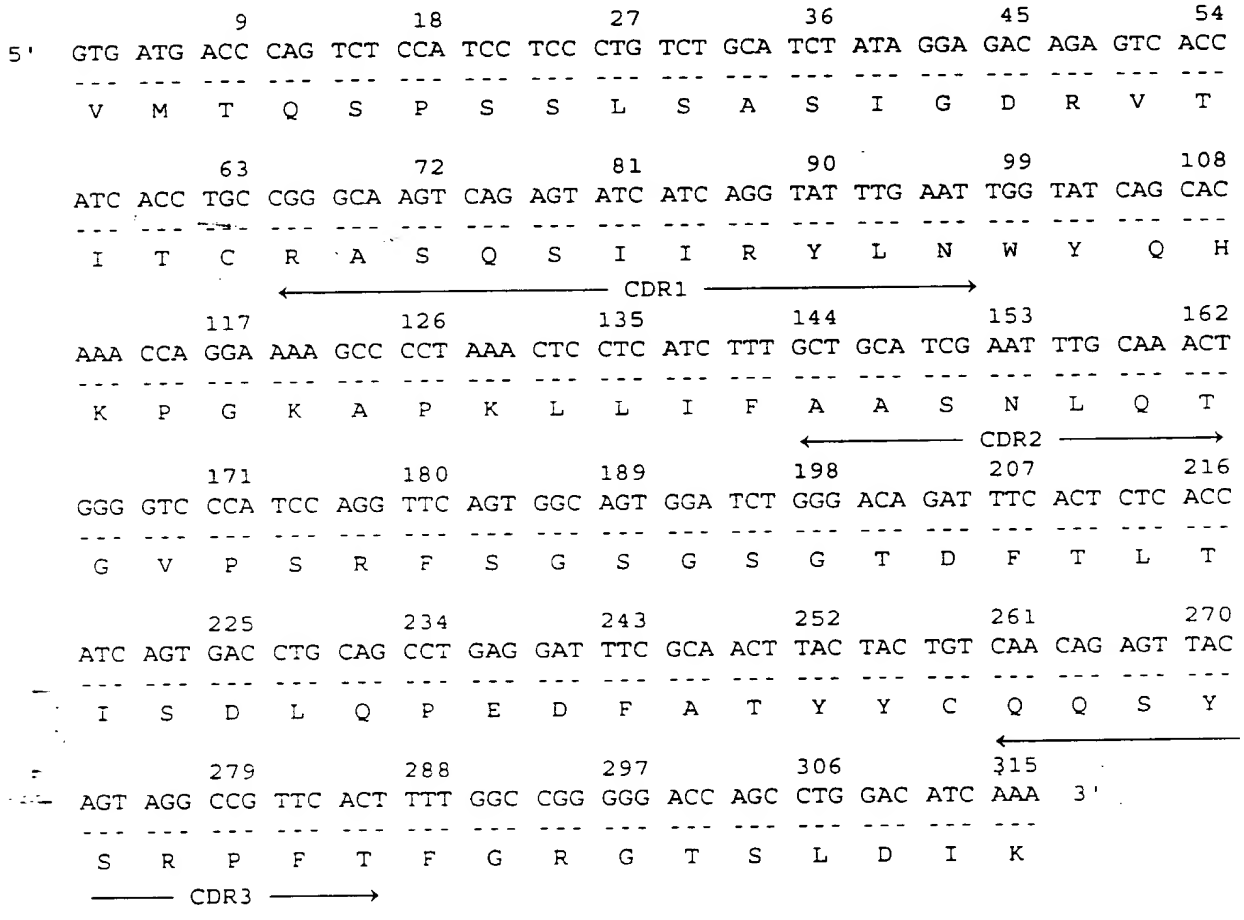


Fig. 5a

LD1-98-VH sequence

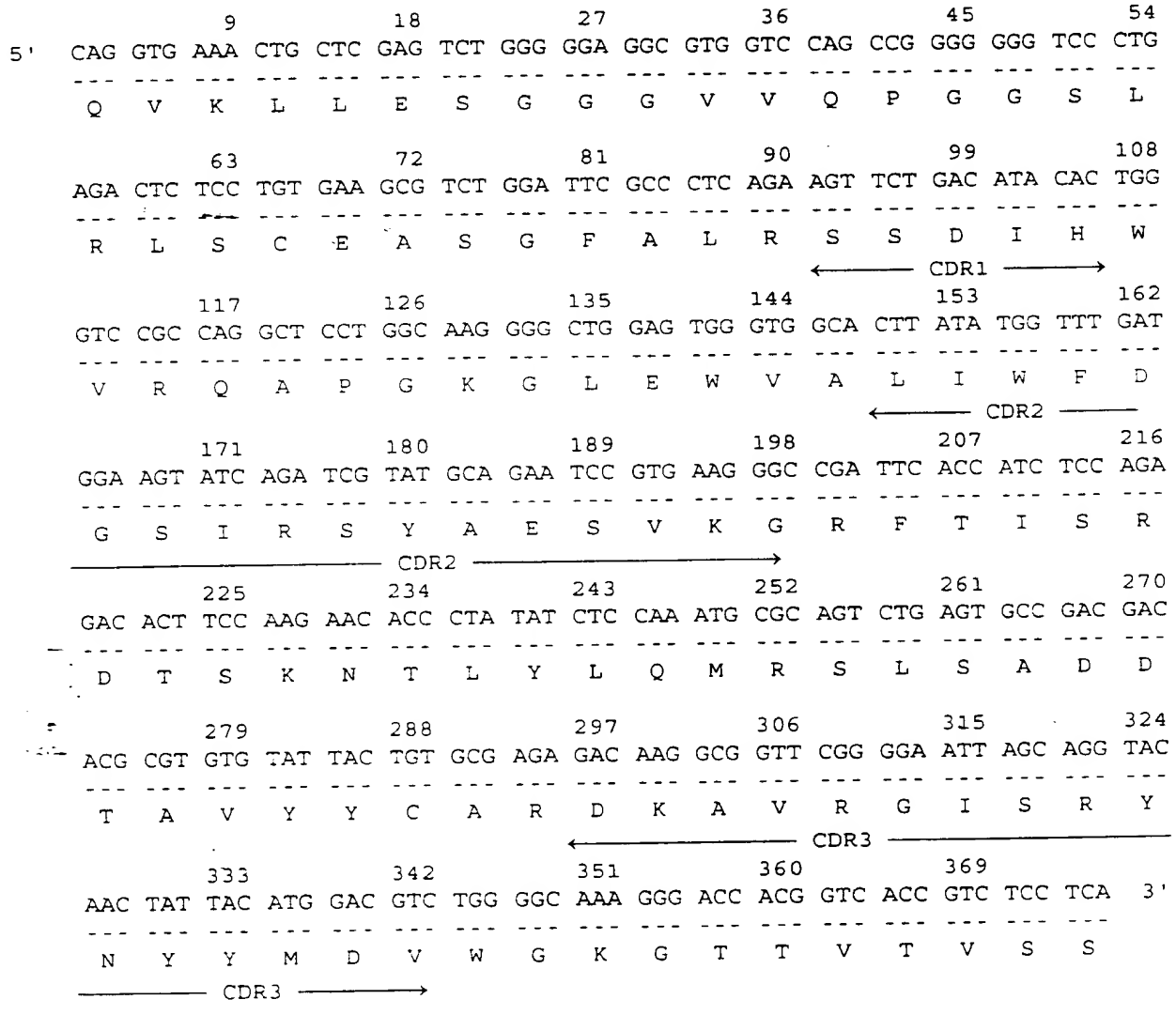


Fig. 5b

LD1-98-VL sequence

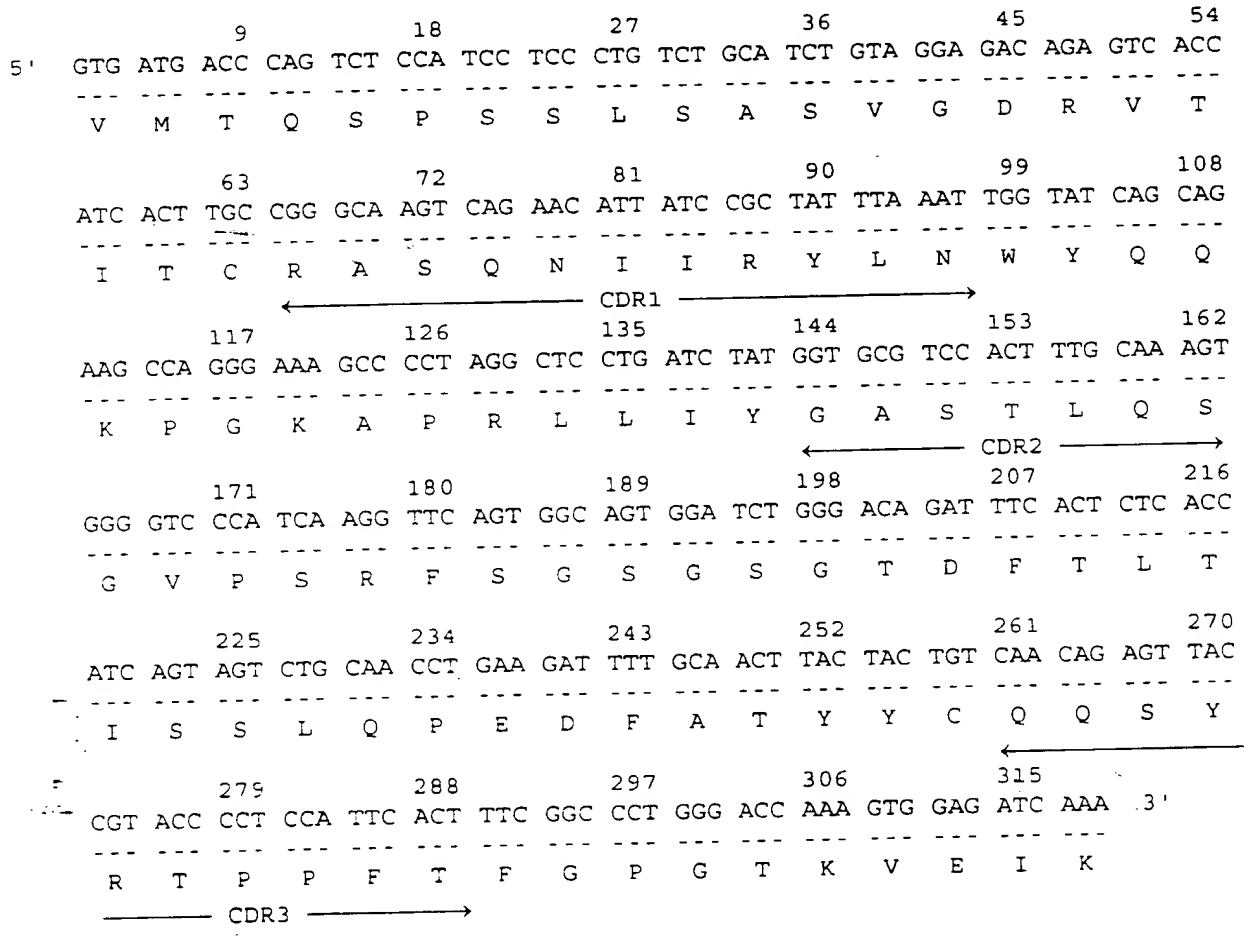


Fig. 6a

LD1-110-VH sequence

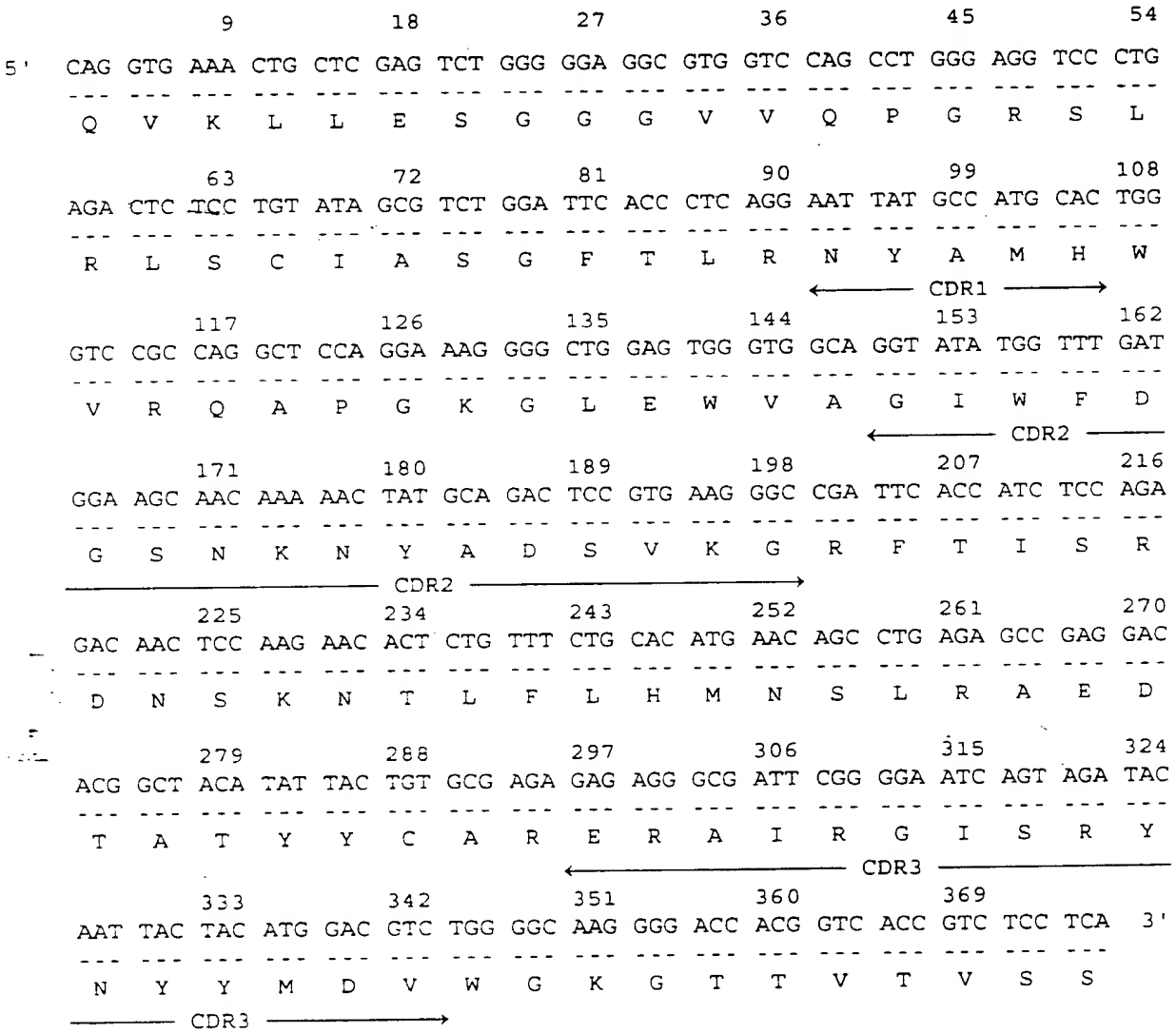


Fig. 6b

LD1-110-VL sequence

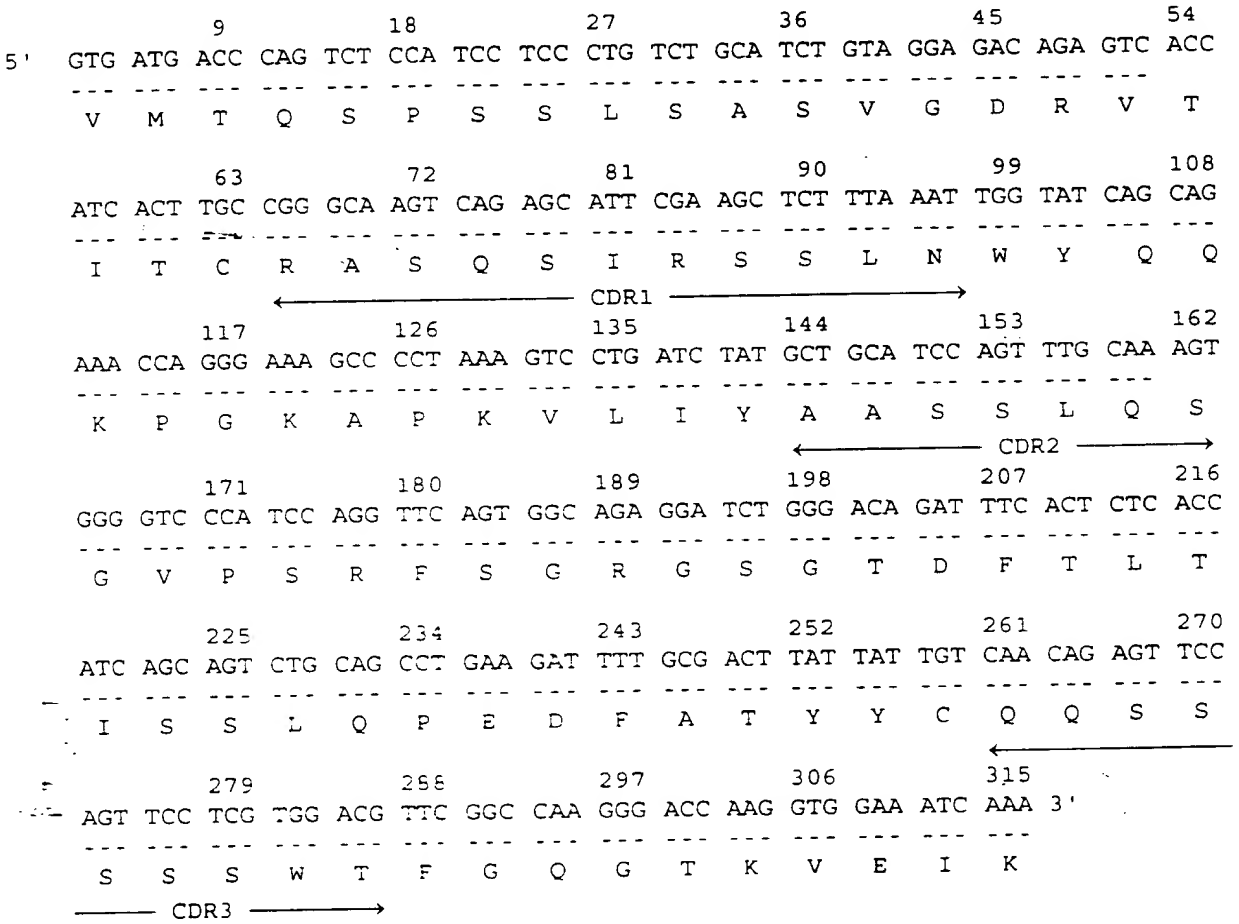


Fig. 7a

LD1-117-VH sequence

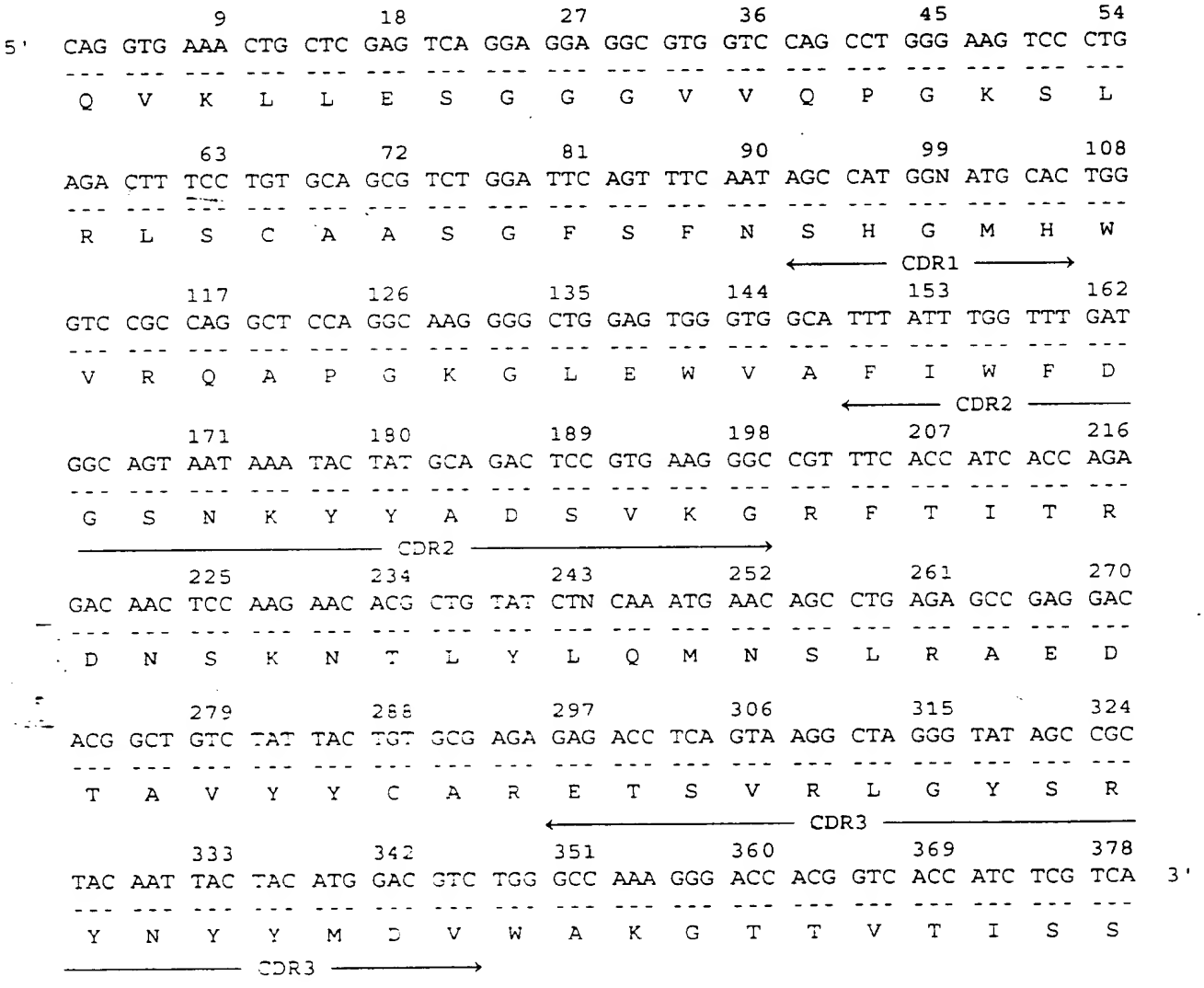


Fig. 7b

LD1-117-VL sequence

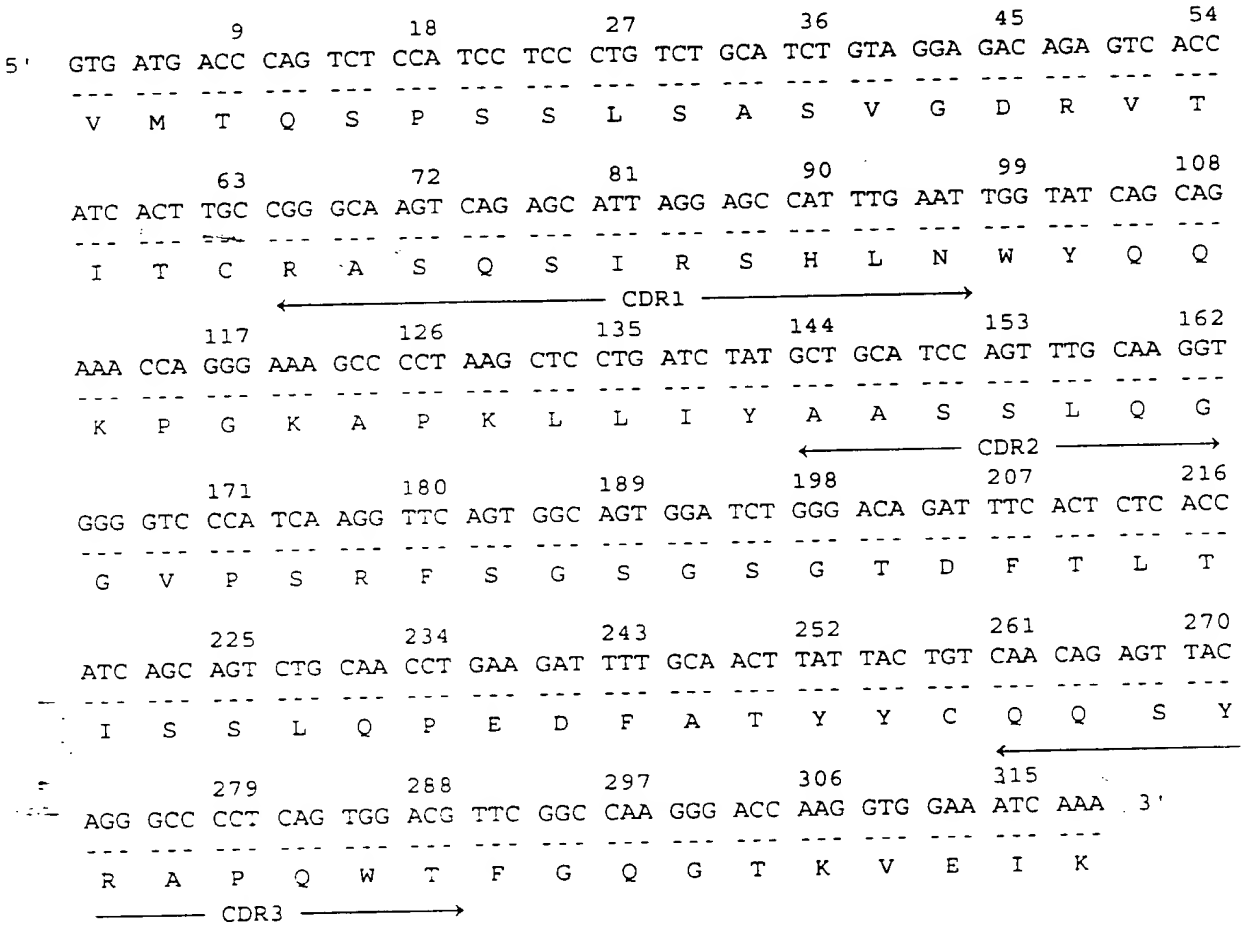


Fig. 8a

LD2-1-VH sequence

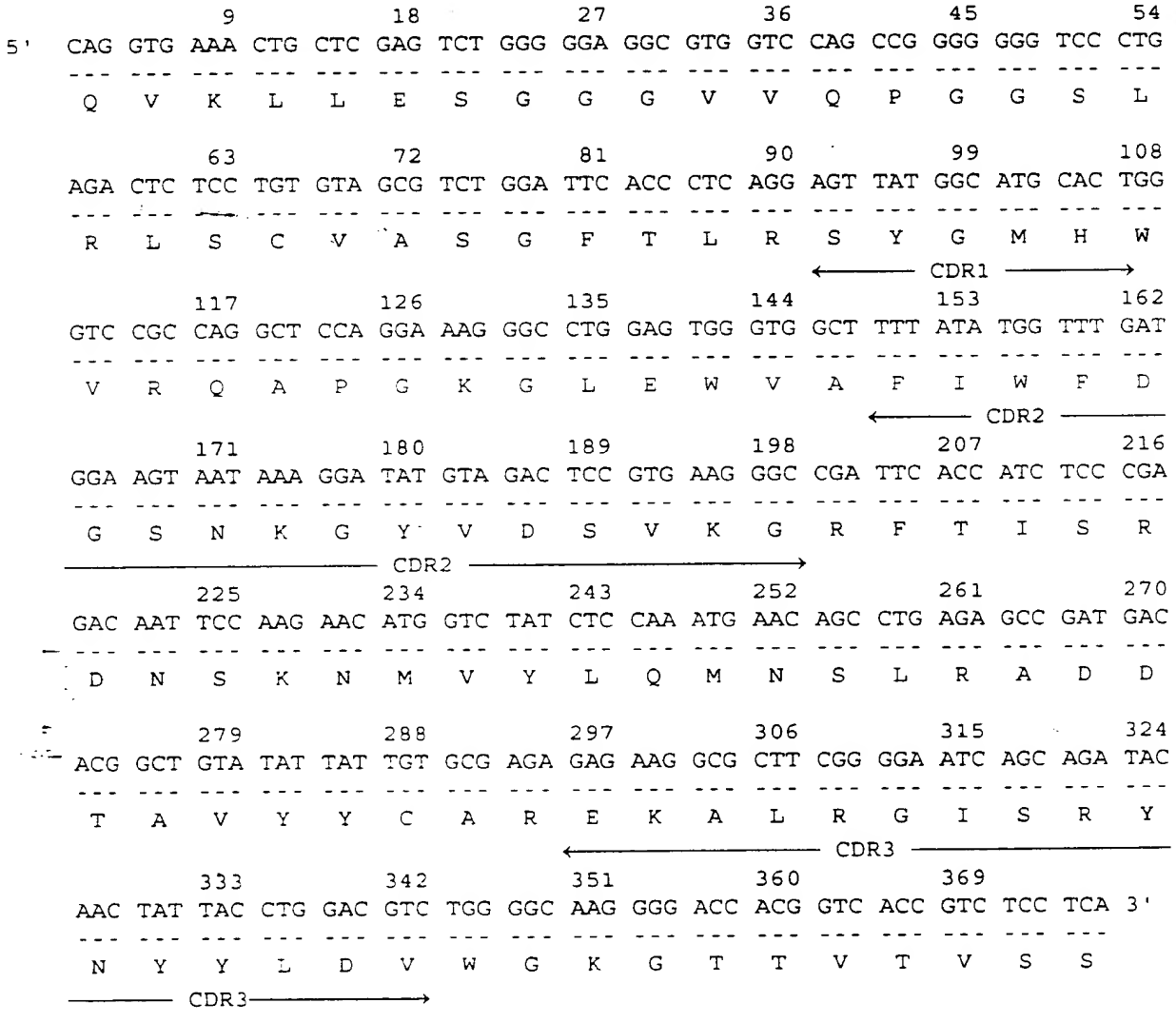


Fig. 8b

LD2-1-VL sequence

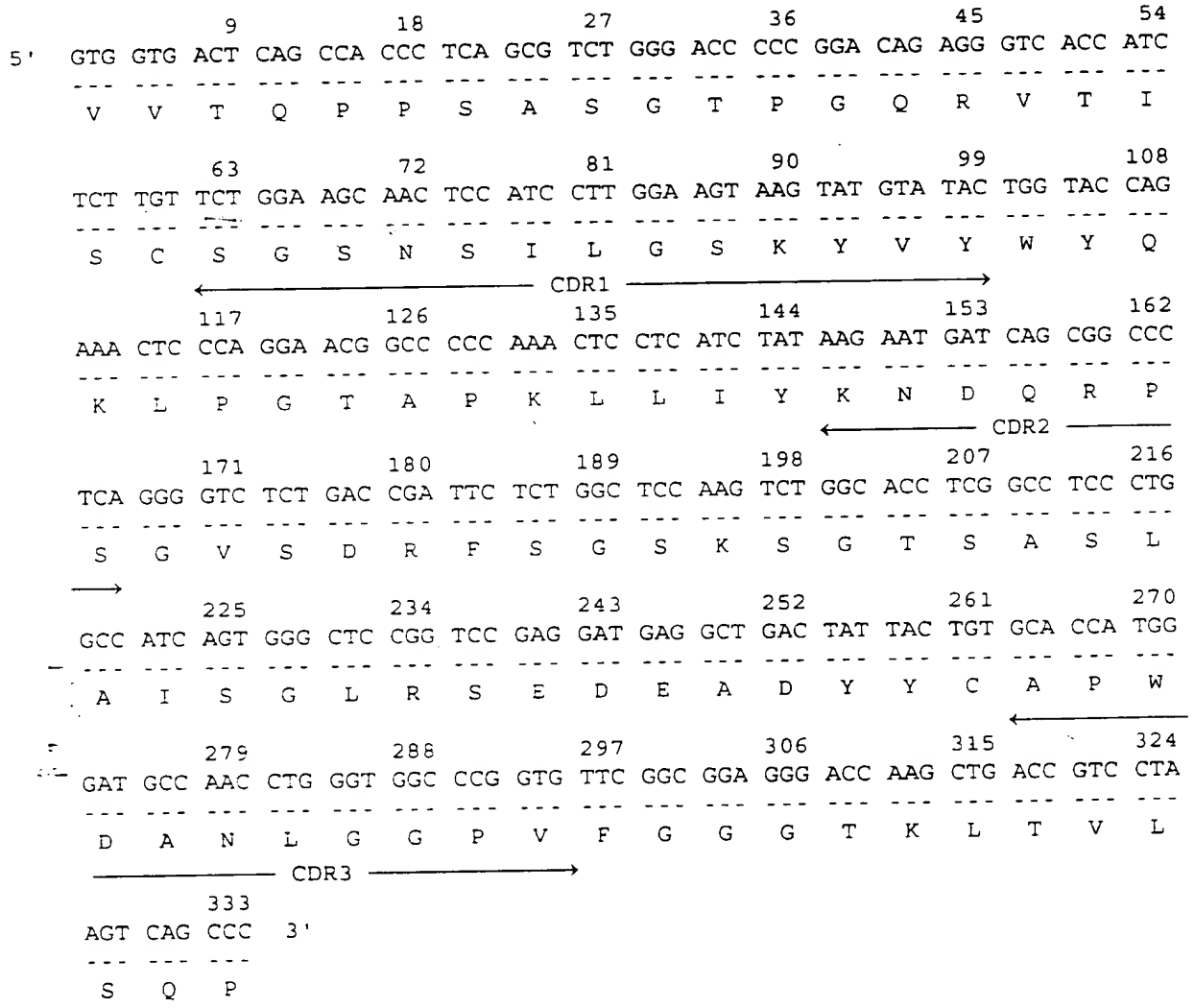


Fig. 9a

LD2-4-VH sequence

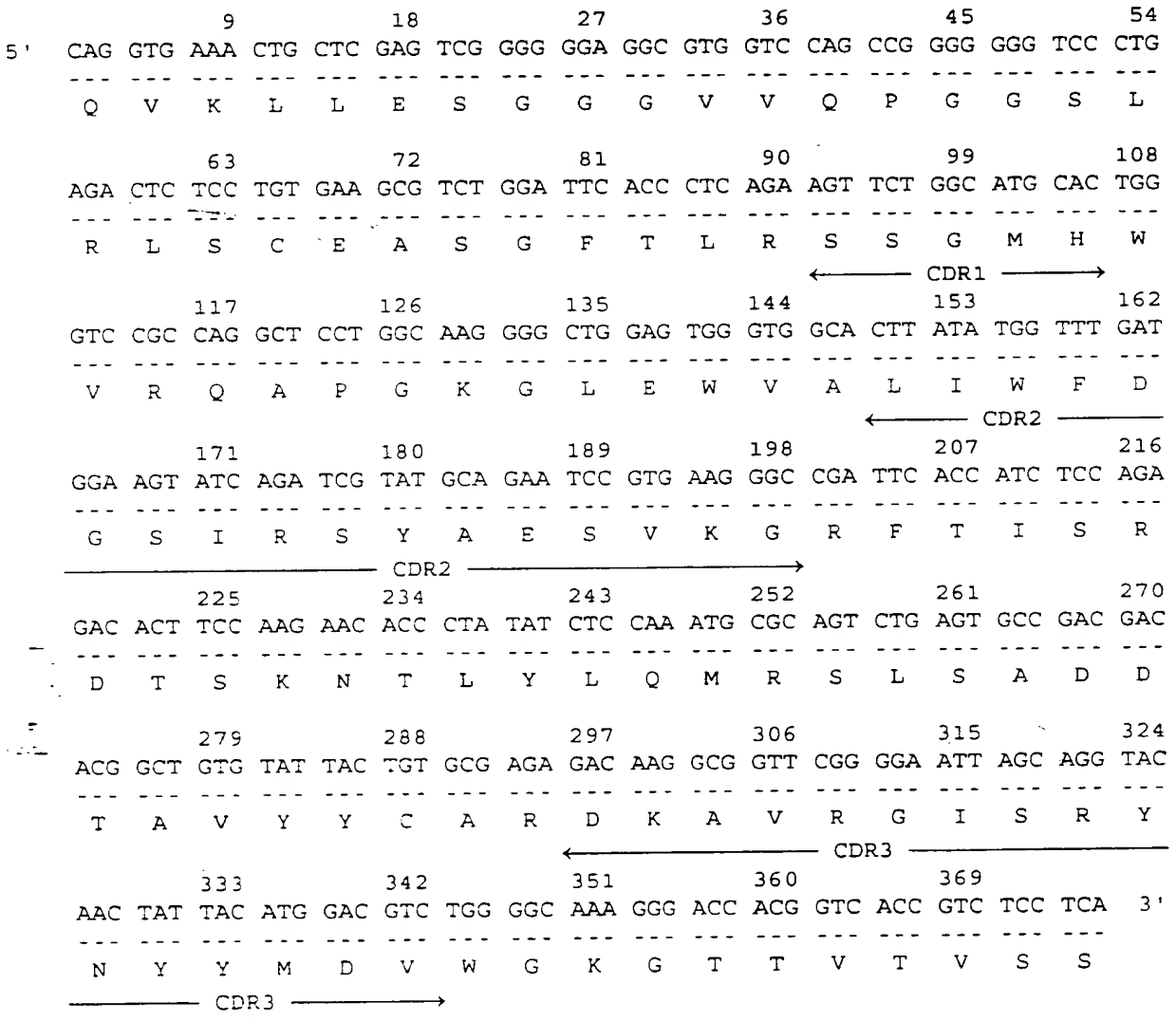


Fig. 9b

LD2-4-VL sequence

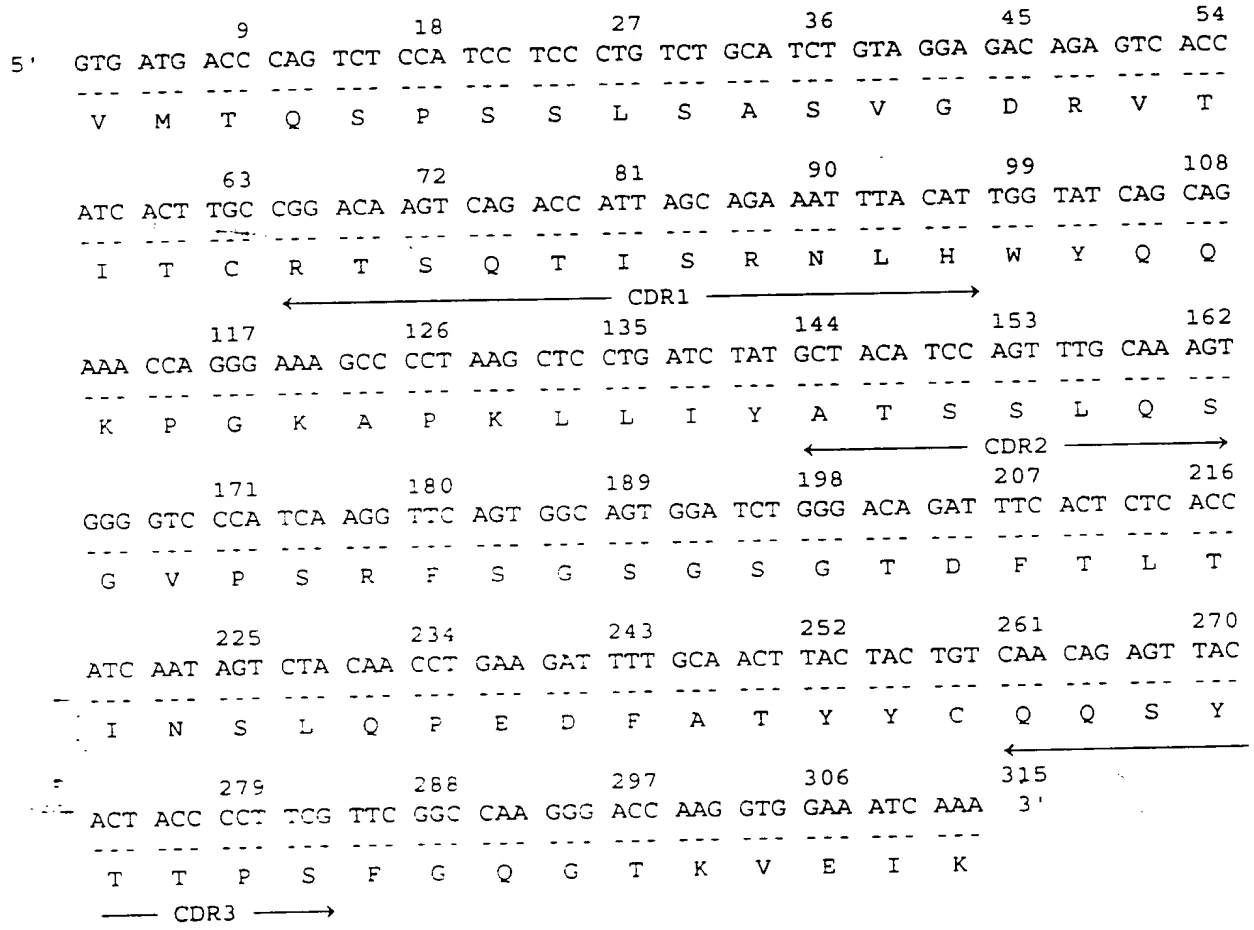


Fig. 10a

LD2-5-VH sequence

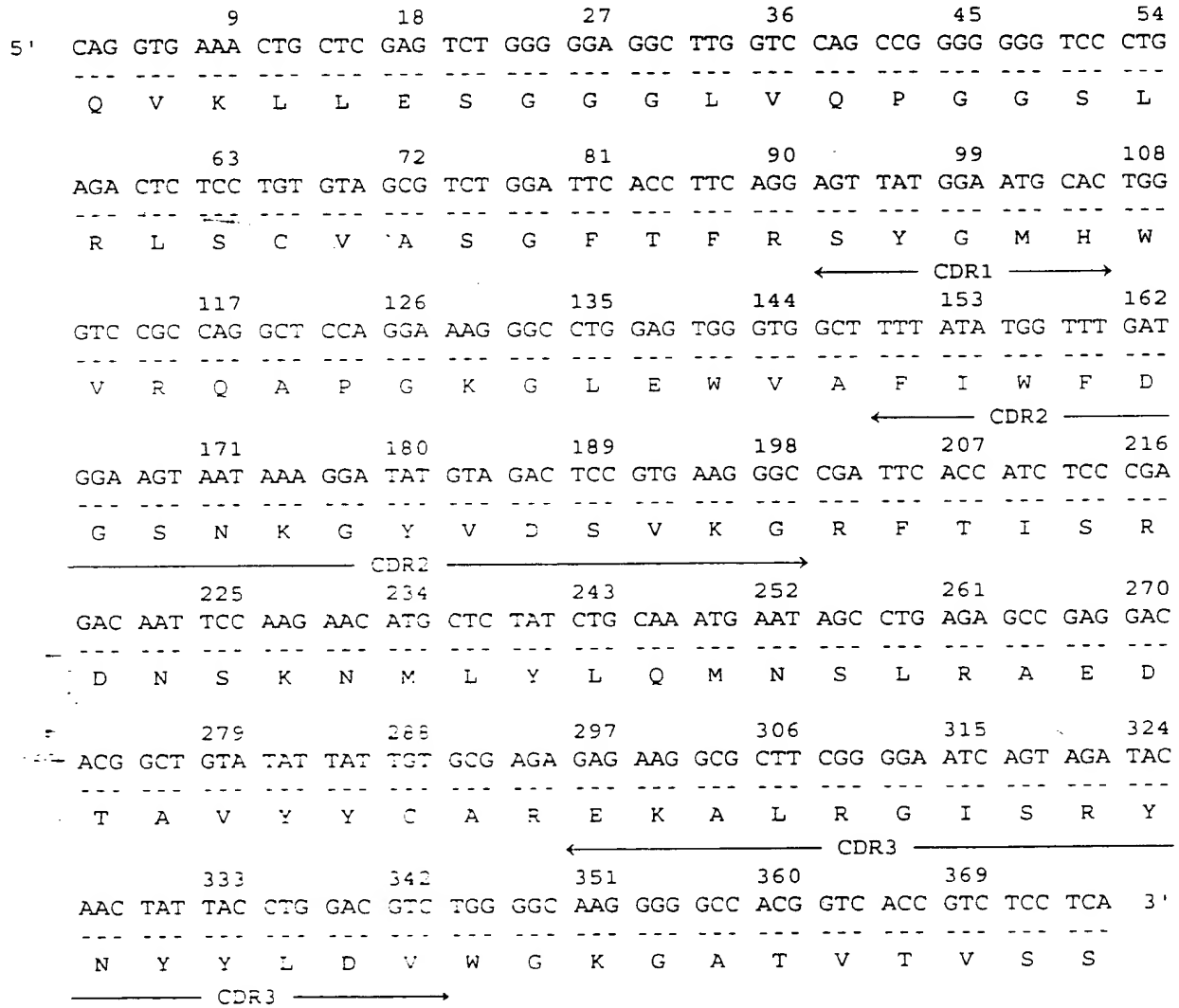


Fig. 10b

LD2-5-VL sequence

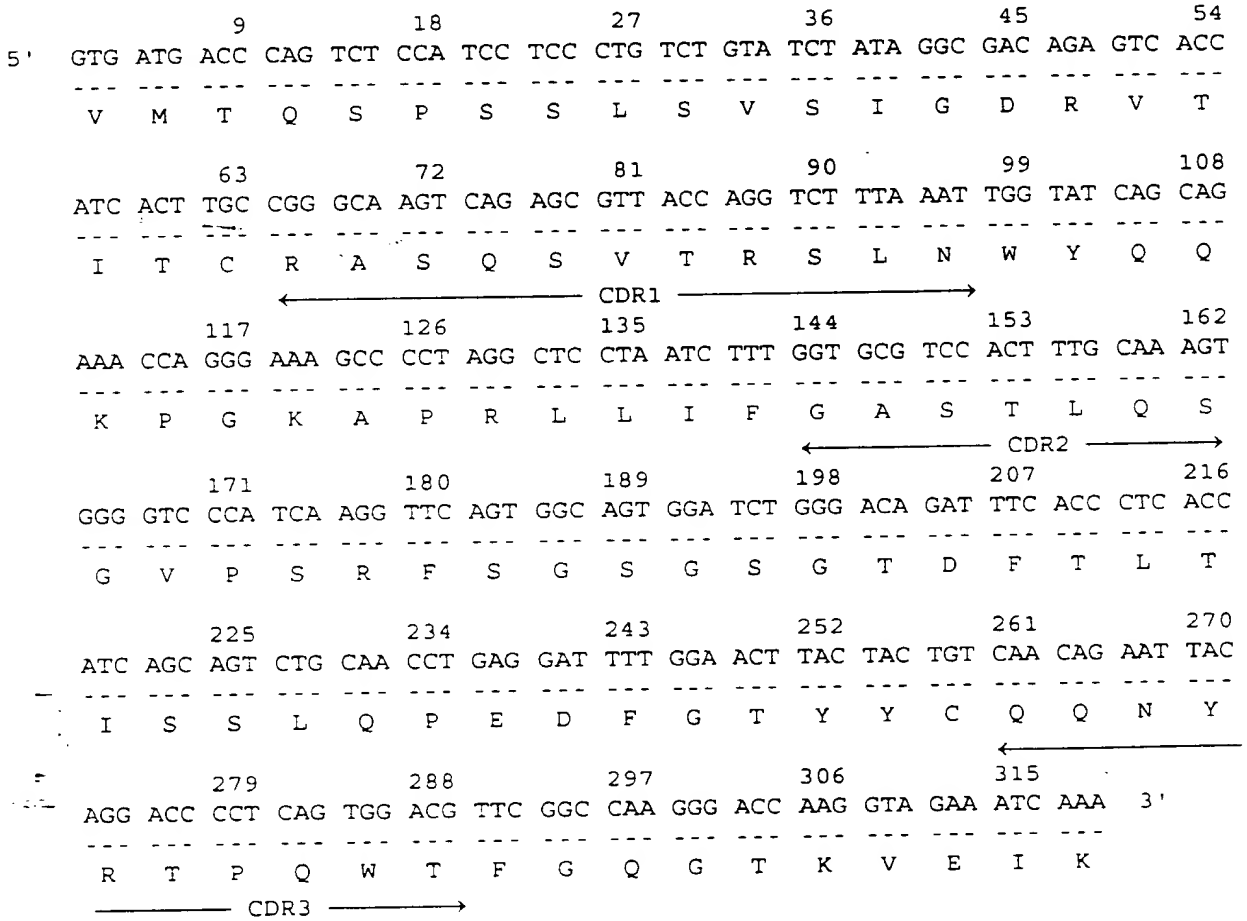


Fig. 11a

LD2-10-VH sequence

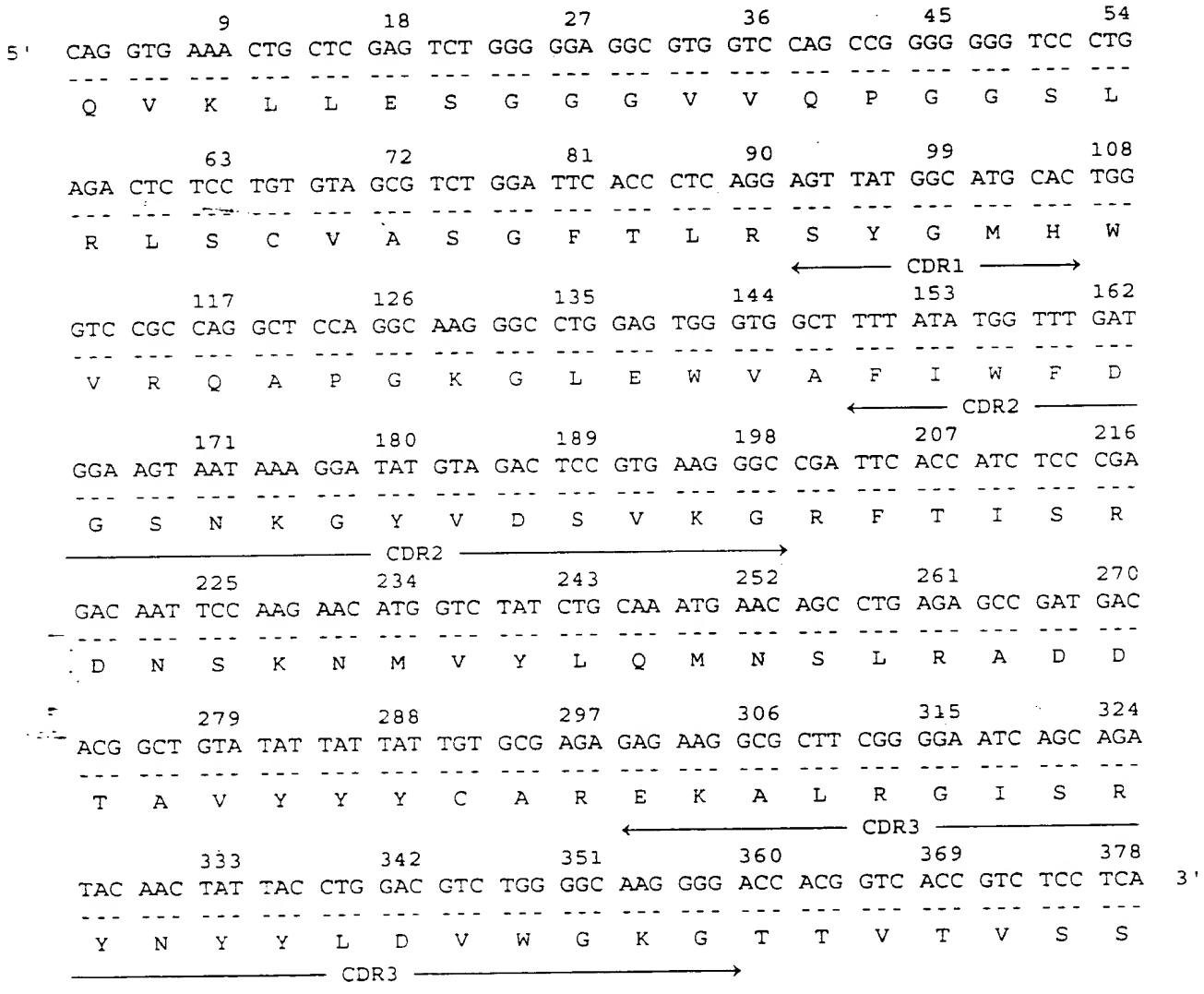


Fig. 11b

LD2-10-VL sequence

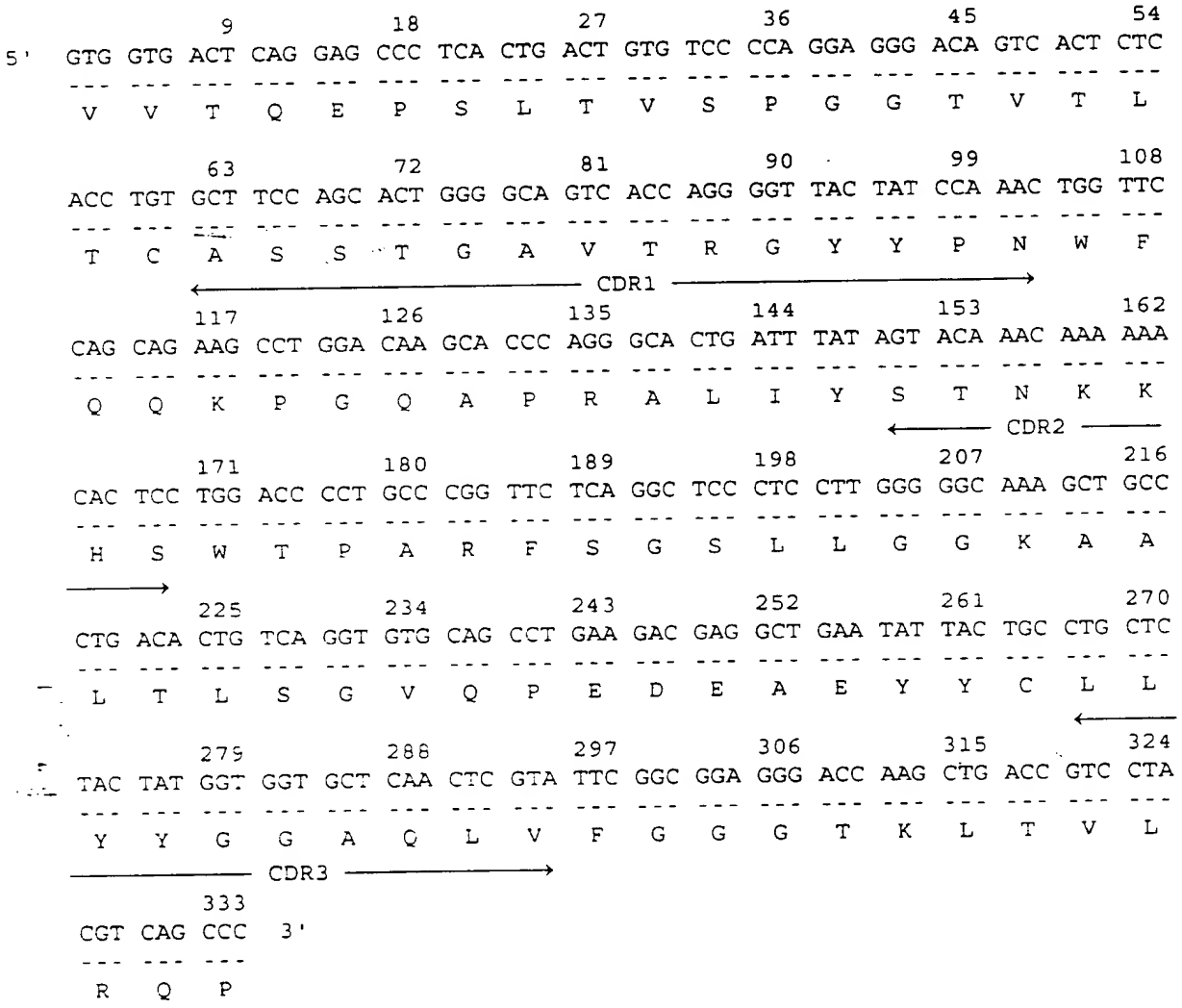


Fig. 12a

LD2-11-VH sequence

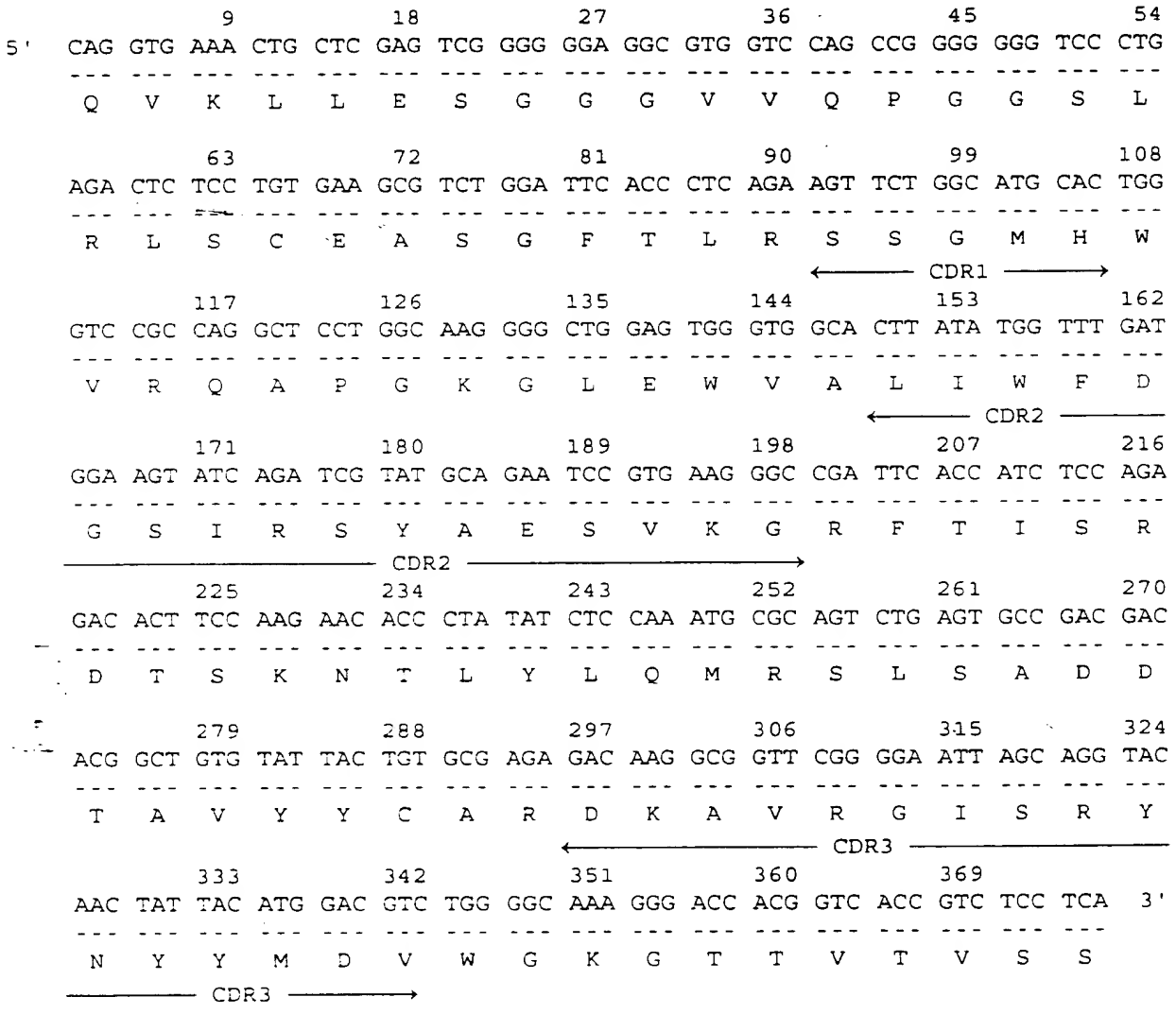


Fig. 12b

LD2-11-VL sequence

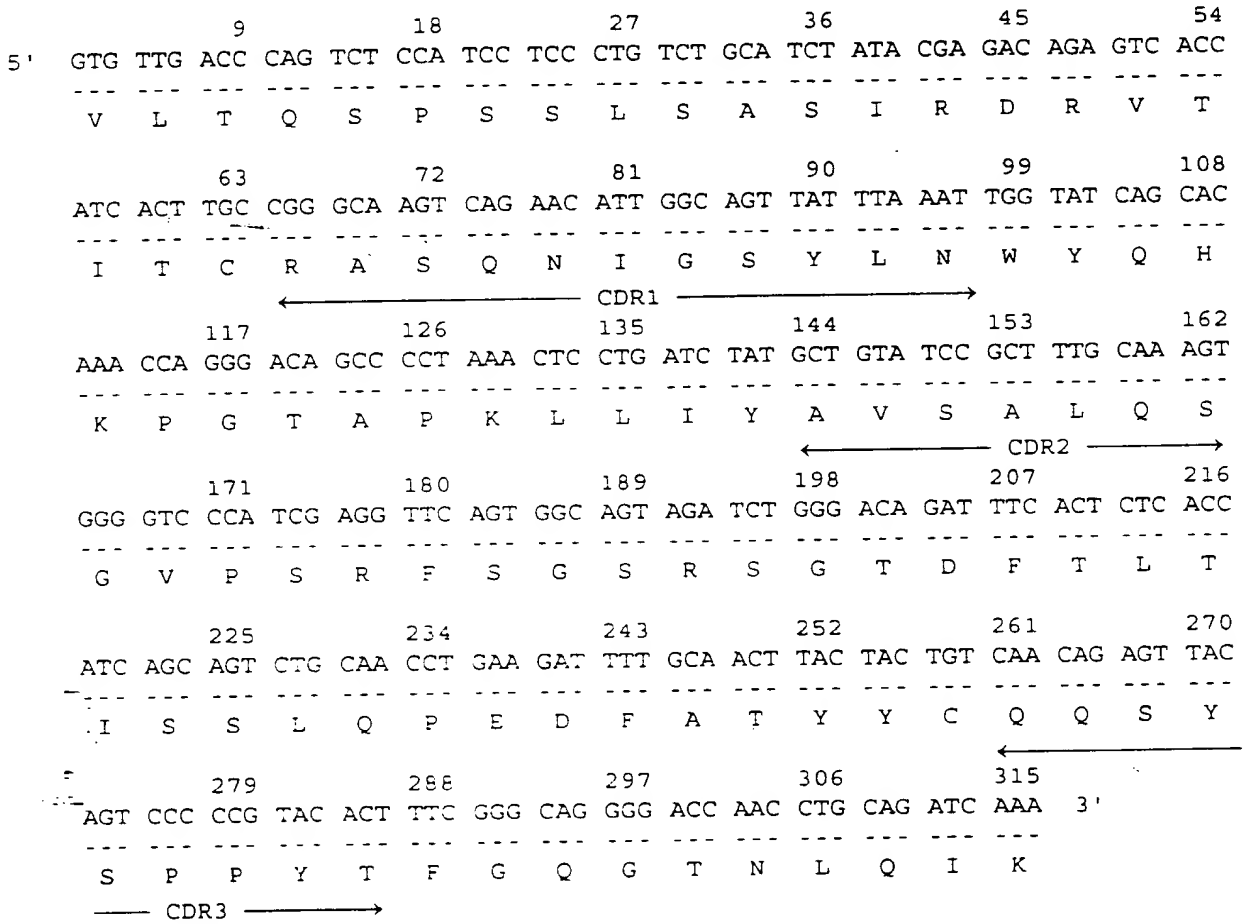


Fig. 13a

LD2-14-VH sequence

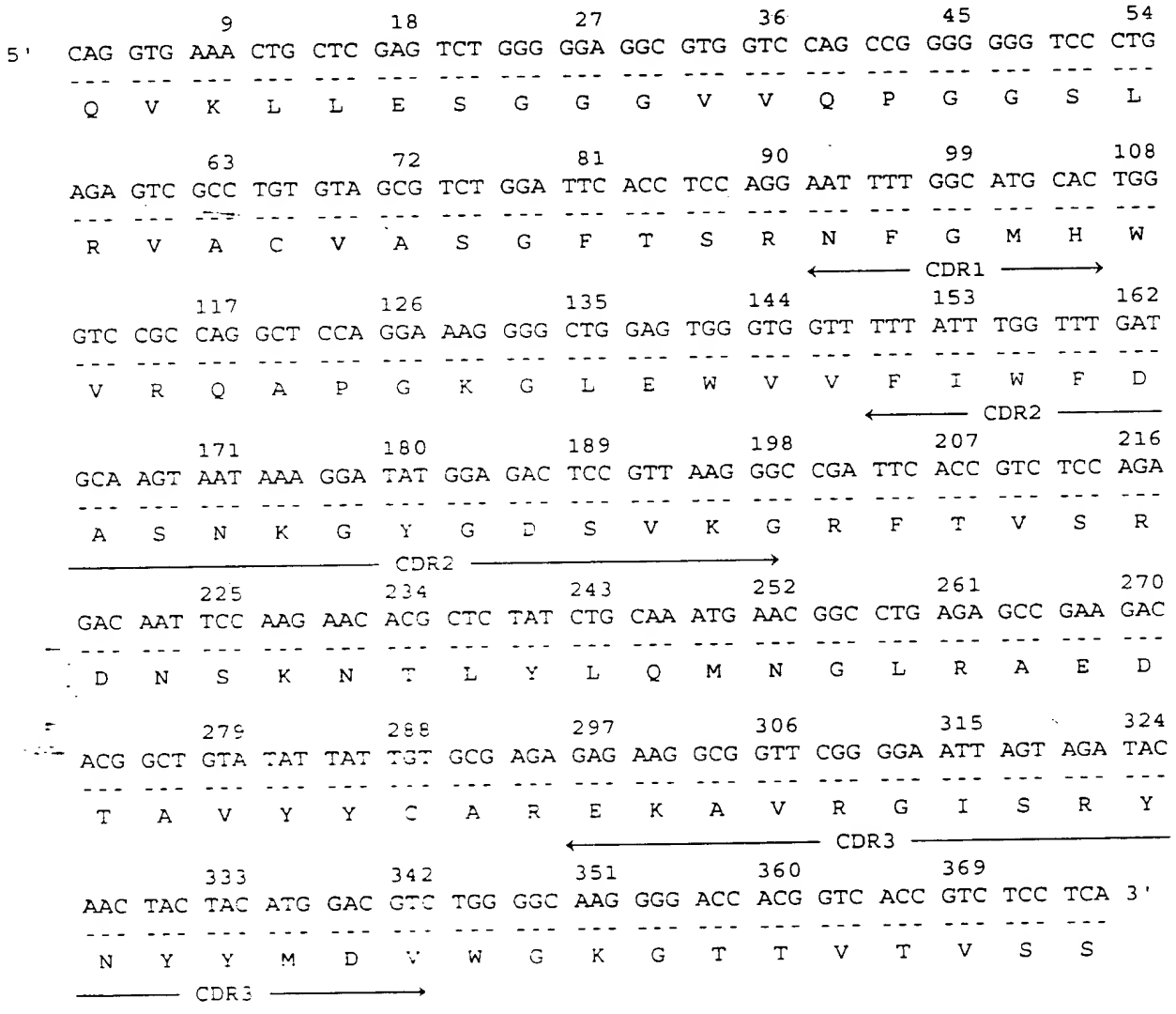


Fig. 13b

LD2-14-VL sequence

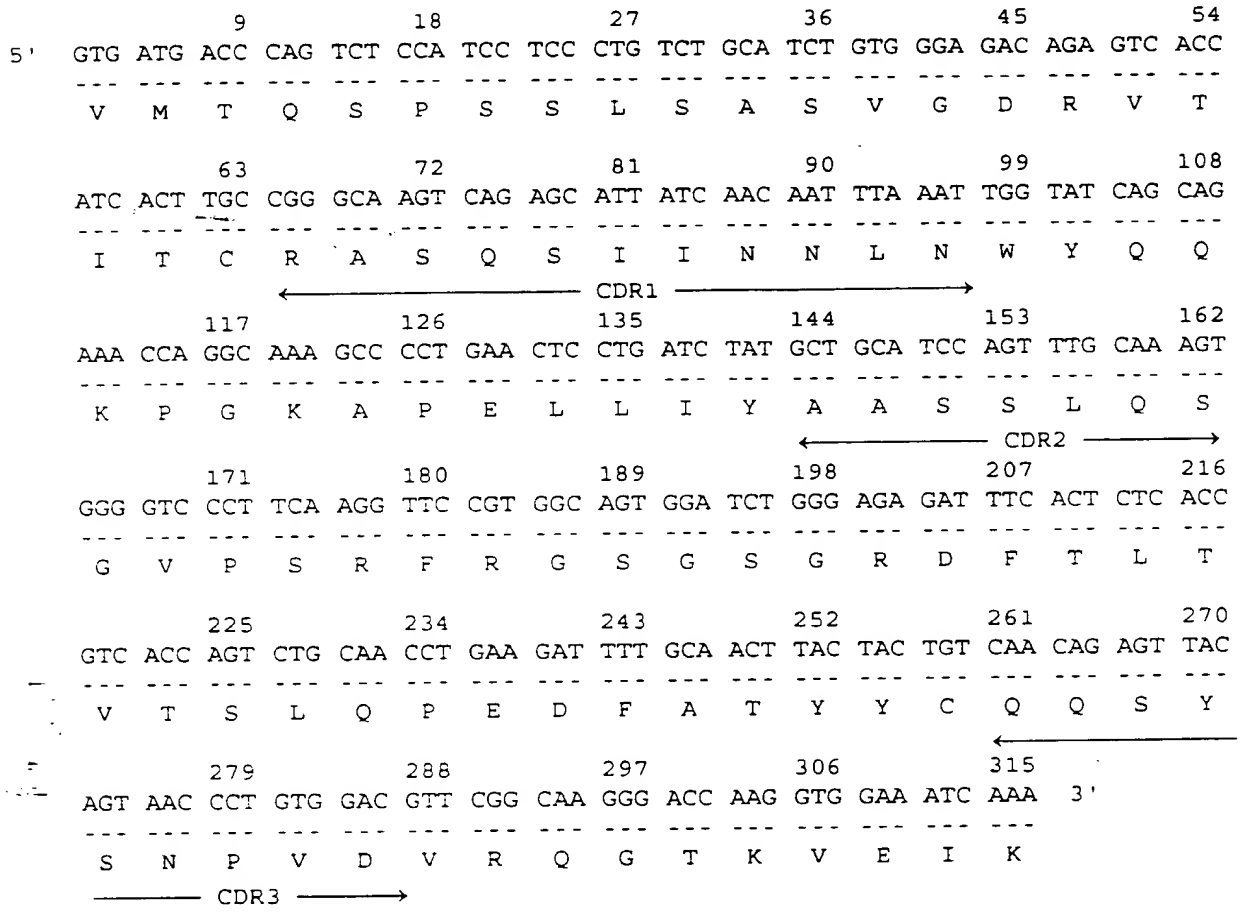


Fig. 14a

LD2-17-VH sequence

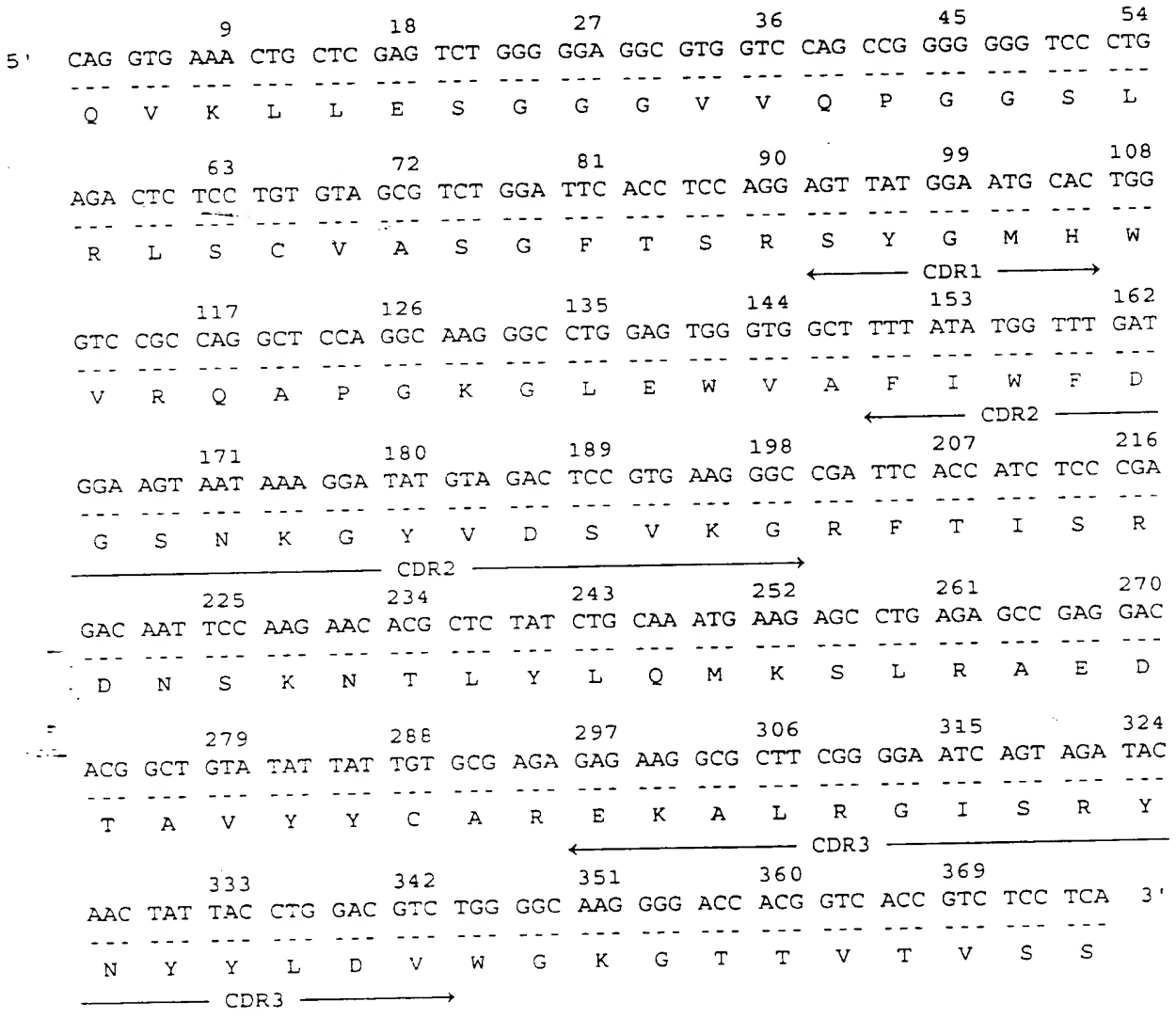


Fig. 14b

LD2-17-VL sequence

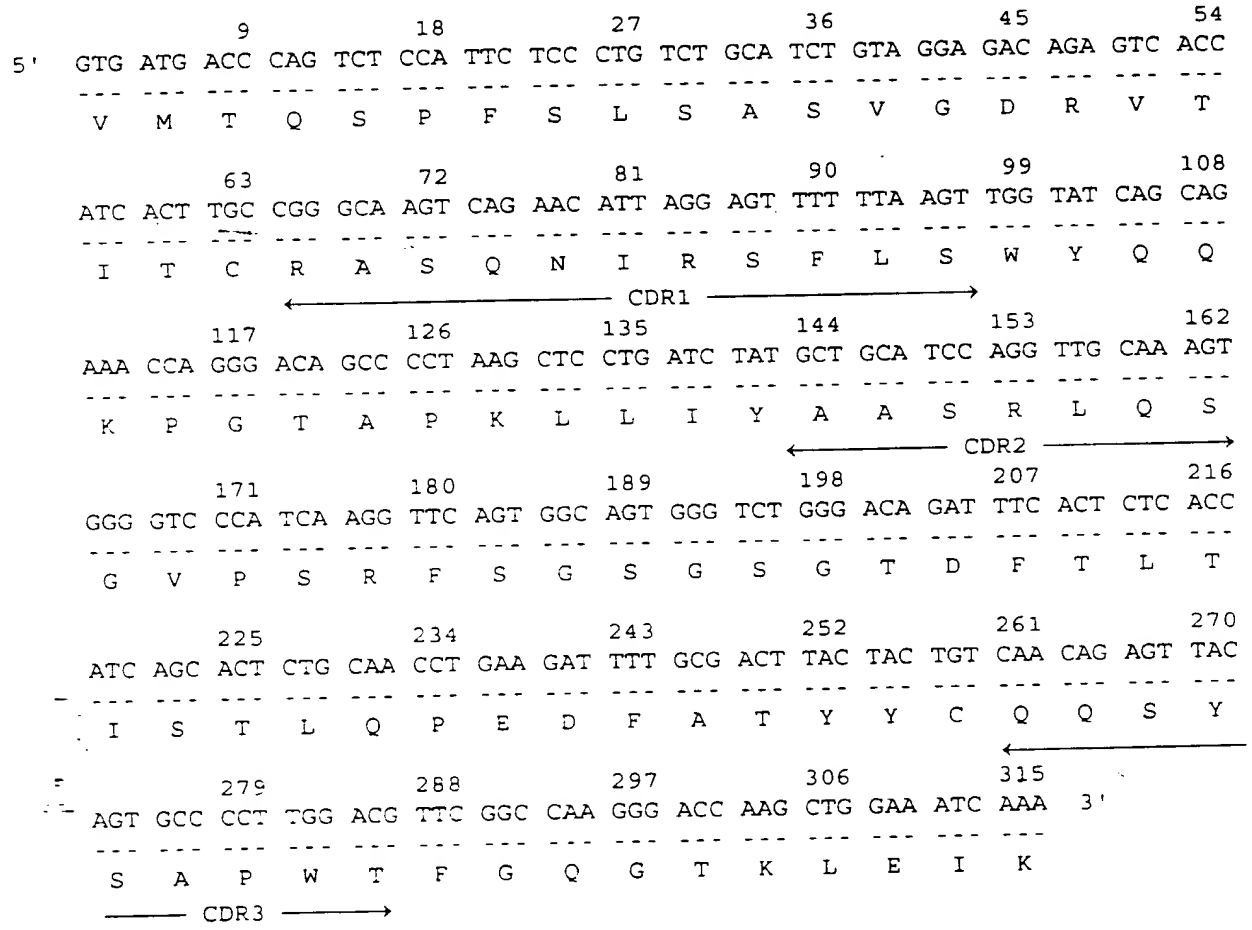


Fig. 15a

LD2-18-VH sequence

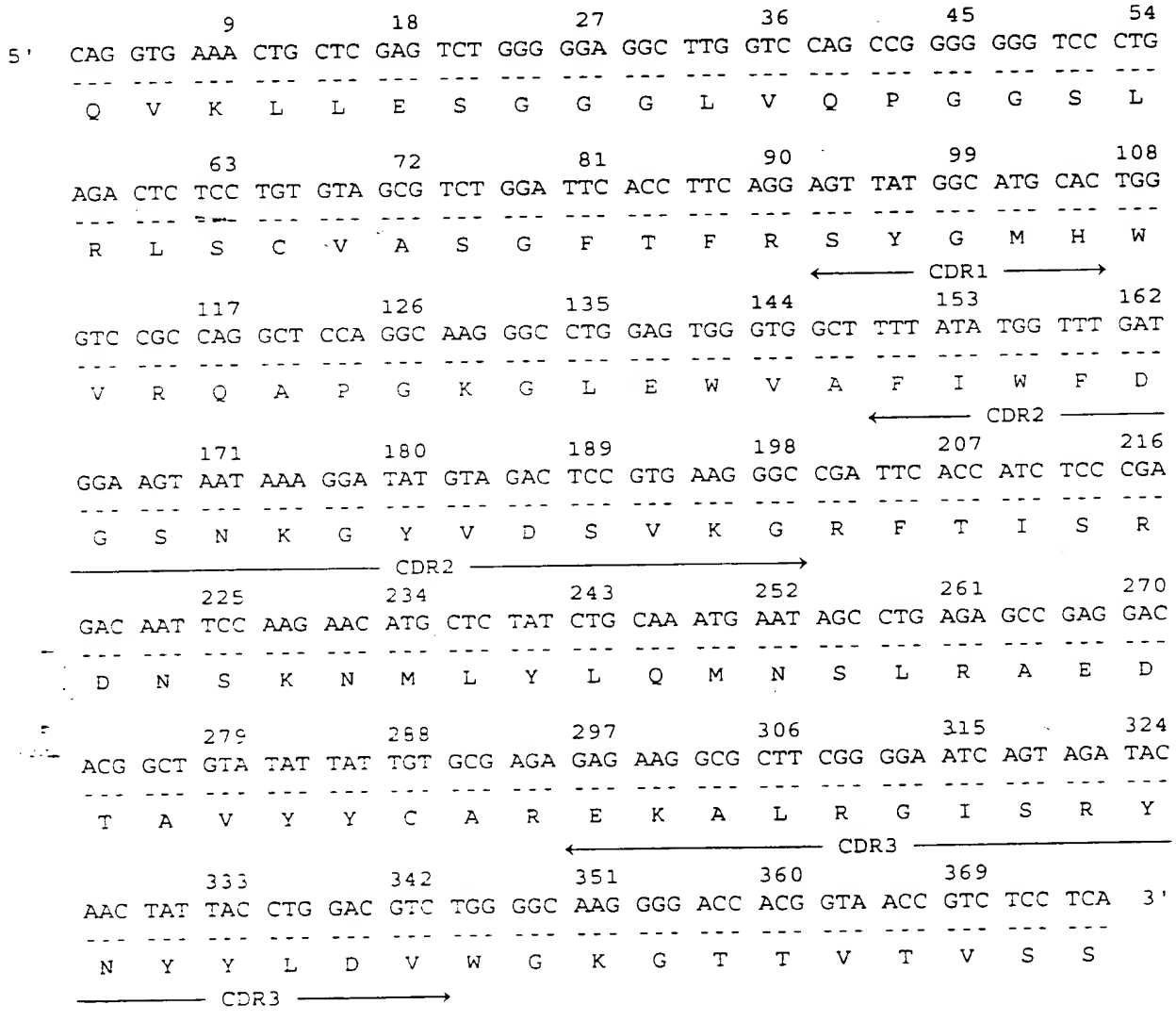


Fig. 15b

LD2-18-VL sequence

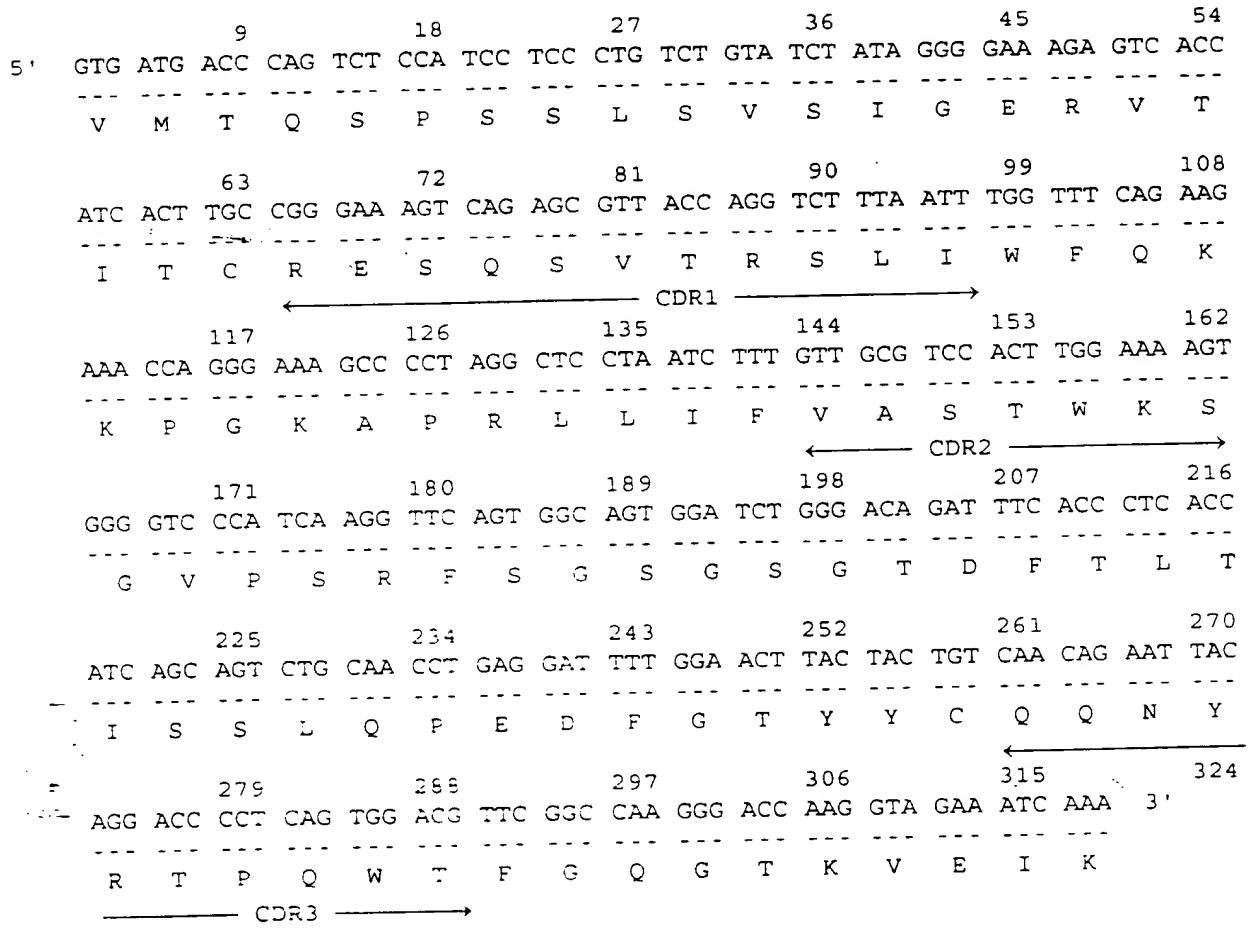


Fig. 16a

LD2-20-VH sequence

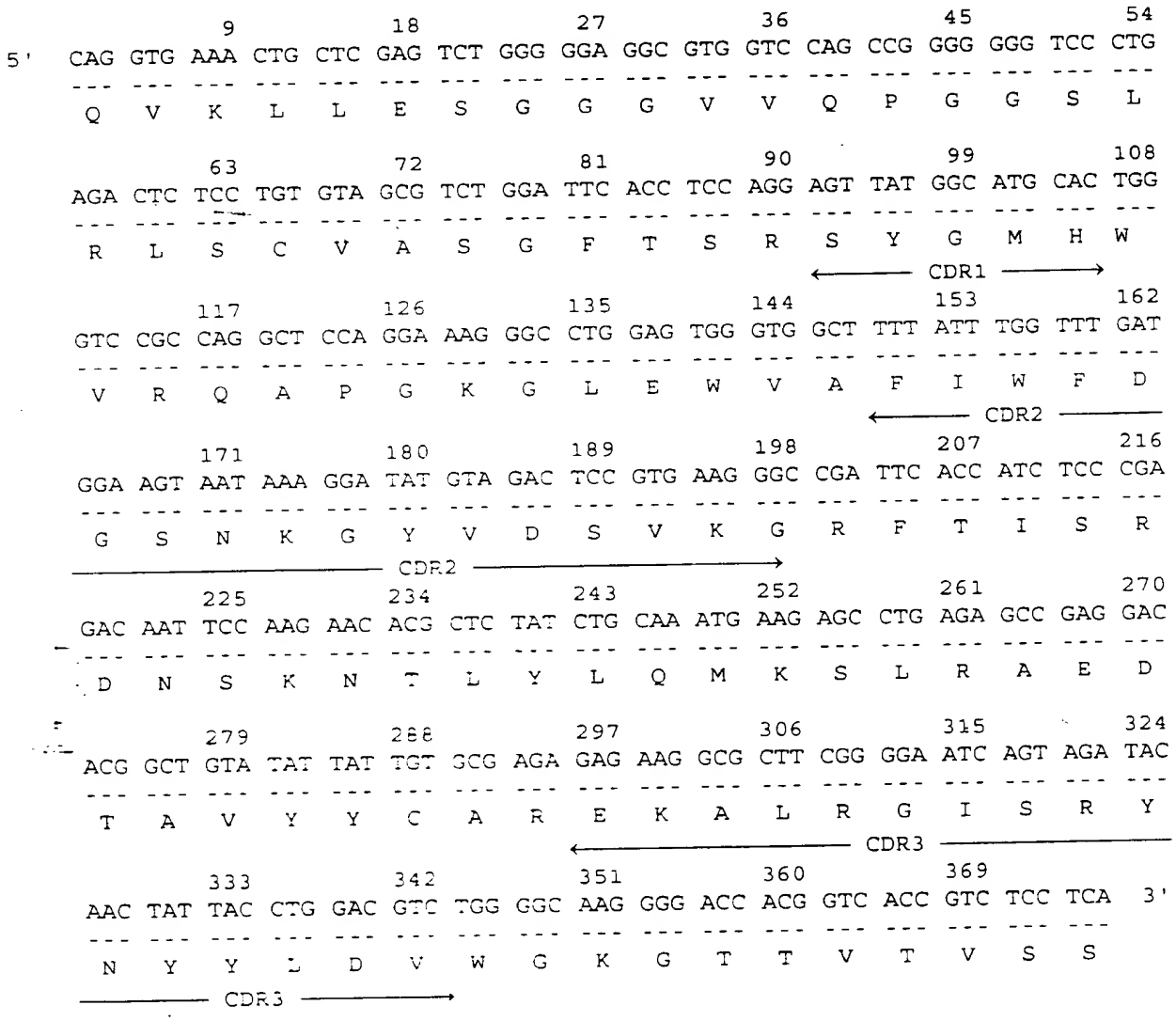


Fig. 16b

LD2-20-VL sequence

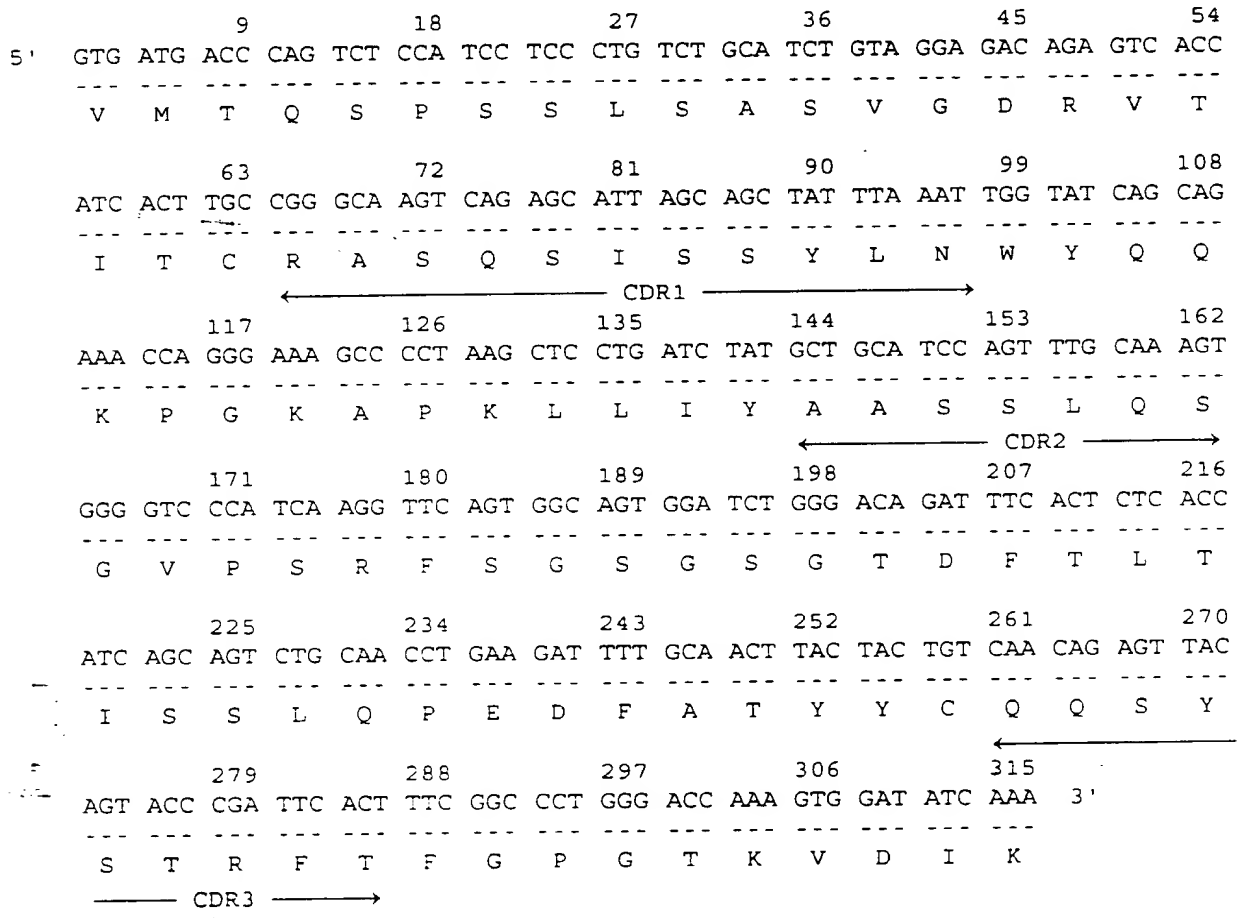


Fig. 17a

LD1-6-17-VH sequence

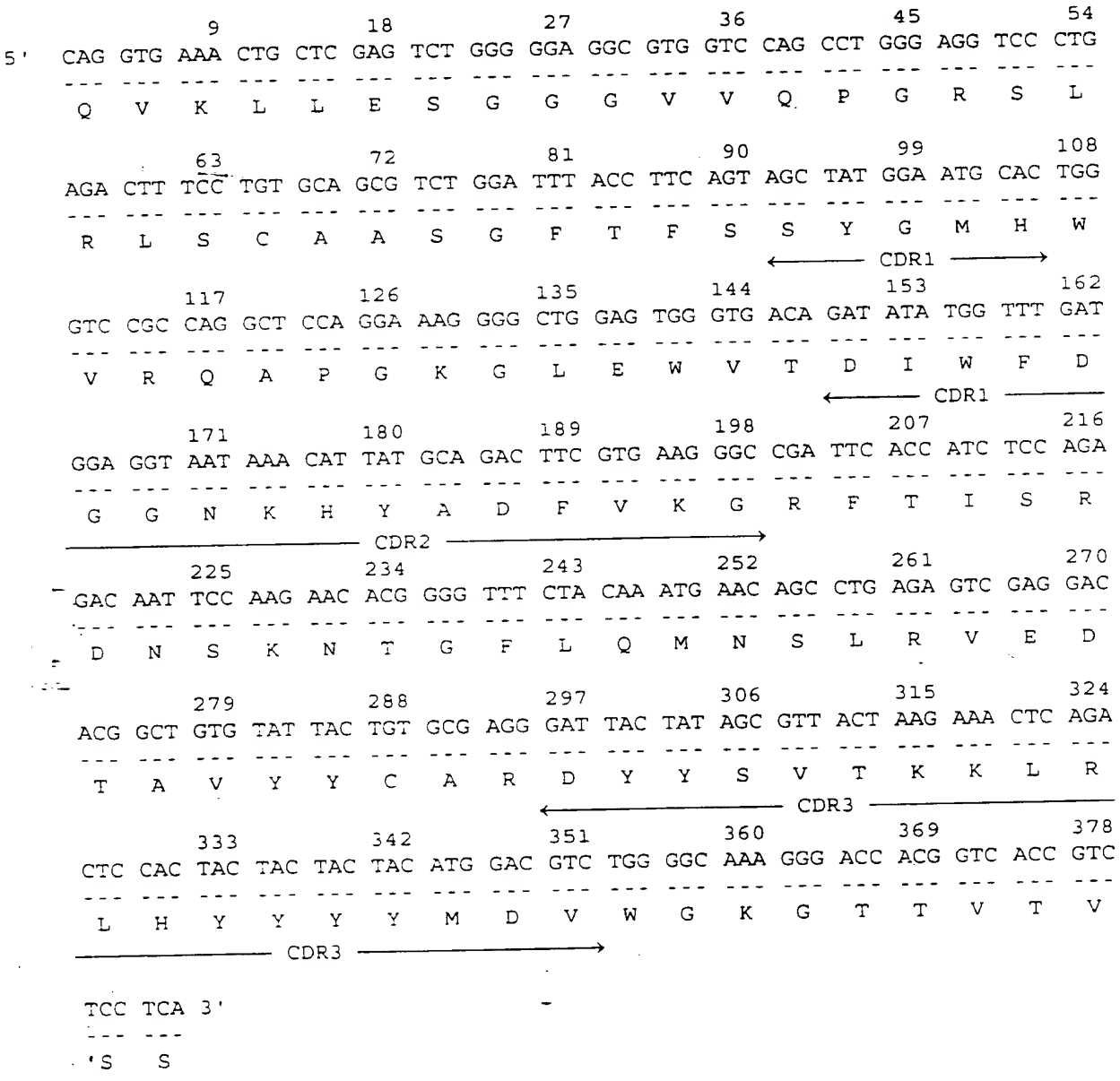


Fig. 17b

LD1-6-17-VL sequence

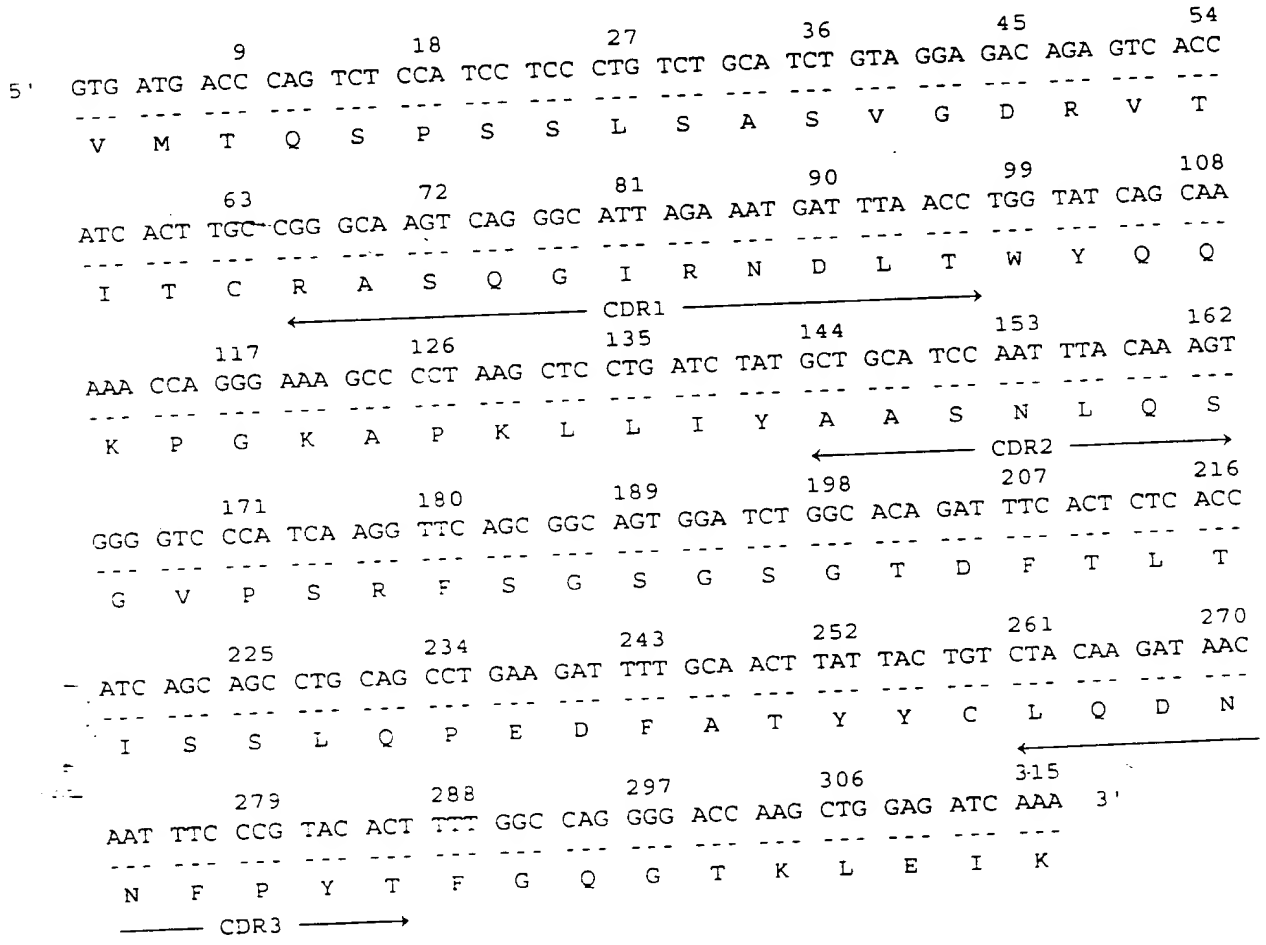
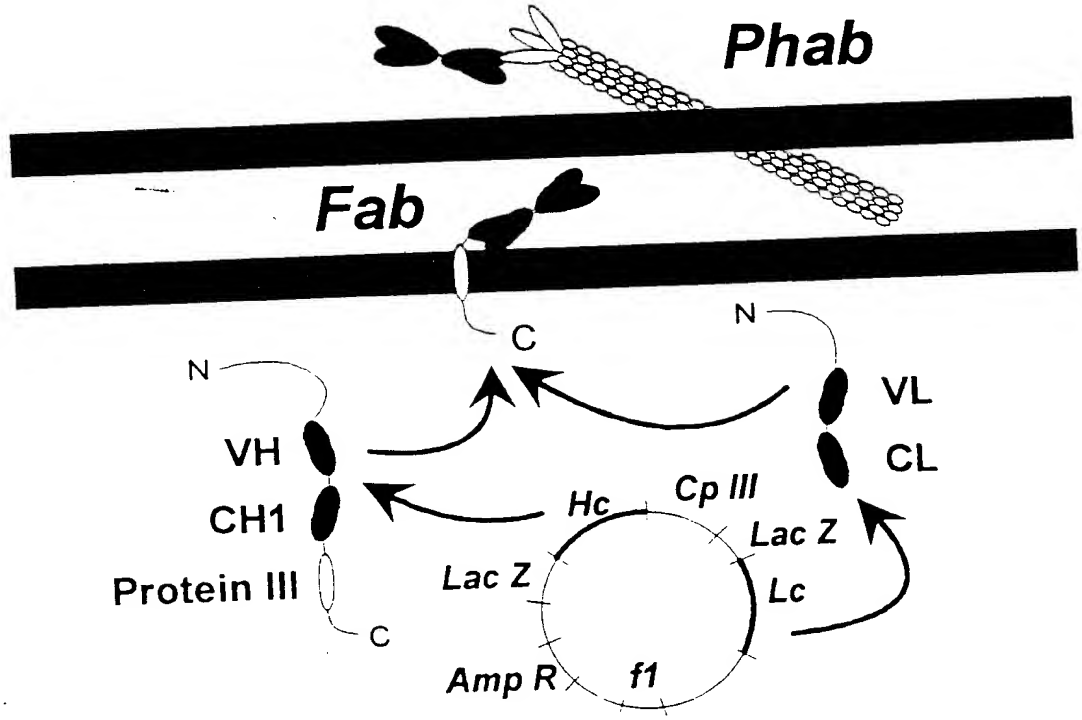
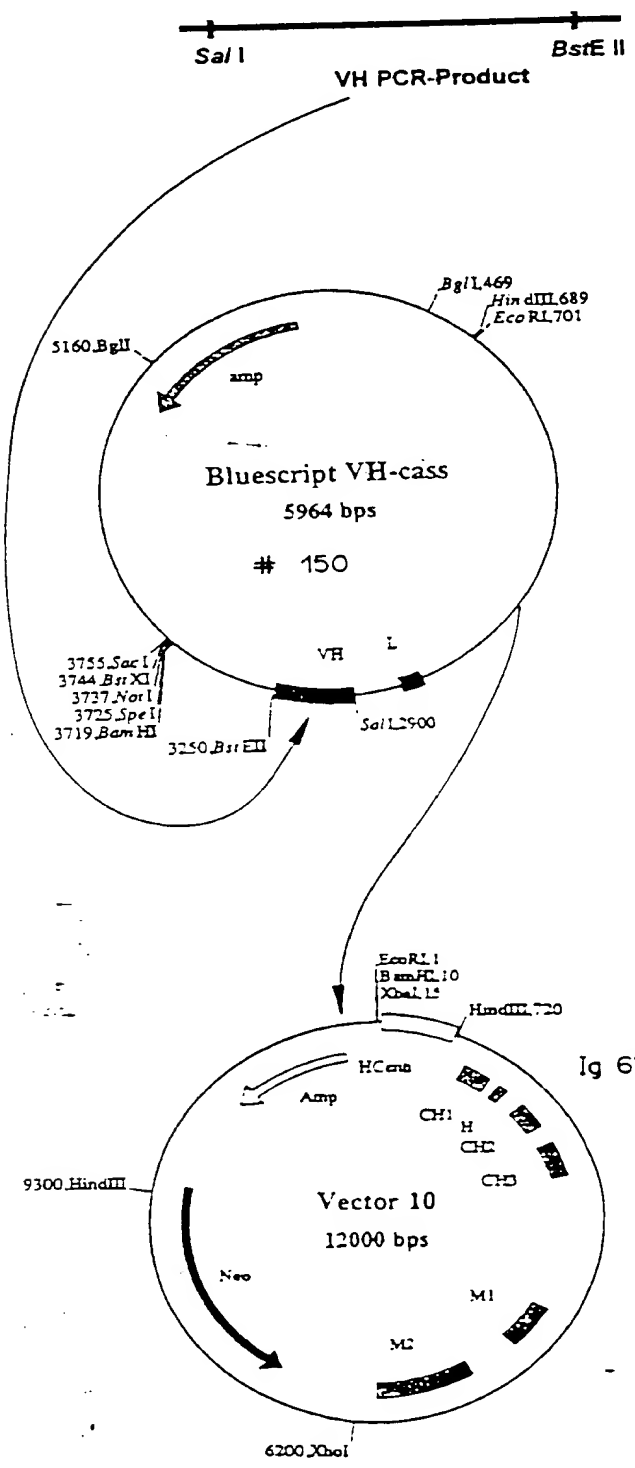


Fig. 18

The pComb3 Expression System





Ig 61

Fig. 19

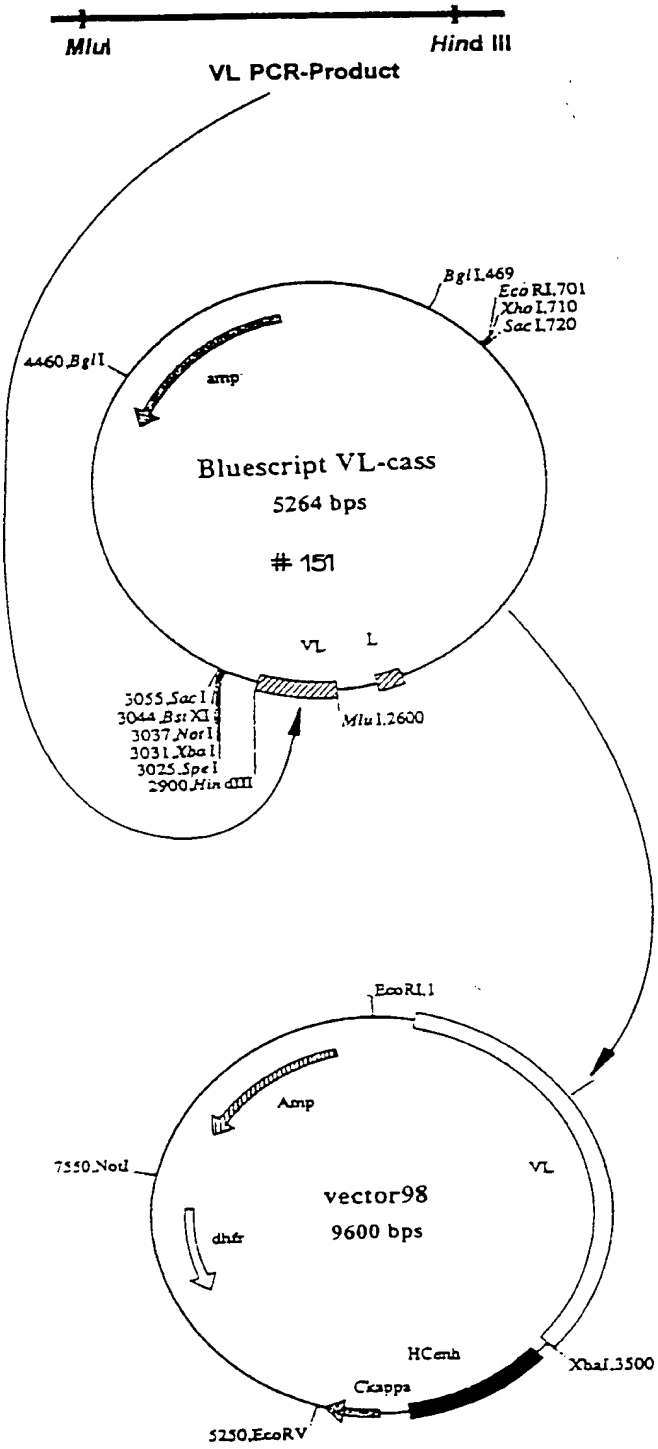


Fig. 20